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EFFECT OF IONIC AND NON IONIC CONTRAST MEDIA ON RED CELL DEFORMABILITY IN VITRO

P ASPELIN

At many points the capillaries have a considerably smaller diameter than the erythrocytes The normal disc shaped erythrocytes pass through the capillaries in single file and have to be bent and deformed to pass through (BRAASCH 1971 BRÅNEMARK & LINDSTRÖM 1963 a b BROWN et coll 1968 GUEST et coll 1963 PROTHERO & BURTON 1962 SKALAK & BRÅNEMARK 1969) It has also been shown in vitro that the red cell is highly deformable by its ability to pass through pores or tubes with diameters smaller than the major cell diameter (BESSIS & MOHANDAS 1975 CHIEN et coll 1971 GREGERSSEN & BRYANT 1968 GREGERSSEN et coll 1967 LINDGARD 1974 a b RAND & BURTON 1964) Thus it is obvious that in the smallest vessels of the microcirculation the red cell deformability and the diameter of the vessel are important determinants of the flow characteristics

Currently used ionic water soluble contrast media are highly hypertonic solutions (1 5-2 5 osm ALMÉN & ASPELIN 1975 ALMÉN et coll 1975) These high osmotic solutions markedly increase whole blood viscosity in vitro (ASPELIN 1978 b) This increase in blood viscosity is due mainly to the effect of the high osmolality on the red cell deformability Thus the normal shear thinning property (decreasing viscosity with increasing shear rate) of blood was reduced or even a shear thickening (increasing viscosity with increasing shear rate) occurred when hypertonic ionic contrast media were mixed with blood This reduction in shear thinning indicates an increased

From the Department of Physiology University of Aachen D-5000 Aachen Germany Supported by the Swedish Medical Research Council Project No 3483 (The author is now at Department of Diagnostic Radiology Malmö Allmänna Sjukhus S-214 01 Malmö Sweden) Submitted for publication 3 February 1978

Table 1

Iodine concentration osmolality and viscosity of the contrast media

Contrast medium	Osmolality (osm)	Iodine content (mg I/ml)	Viscosity (cps) 37 C
Isopaque Cerebral	1 5	280	4 0
Amipaque	0 5	280	5 0
Amipaque	0 3	170	1 8
Urografin 60 *	1 5	290	4 5
Dimer X	1 1	280	7.2

simultaneous measurements of plasma and cell suspensions in triplicate The driving pressure was 50 mm H_2O corresponding to a shear stress of 442 dyn/cm² ($t_w = \Delta P$ R/L 2) where t_w = wall shear stress ΔP = pressure difference R = radius and L = length of the tube) similar to those measured in the capillaries

Selection of the sieve SCHMID-SCHONBEIN et coll (1969) demonstrated that the standard deviation of the pore diameter was approximately ±10 per cent and the variation in flow rate of filtered plasma through the sieves was 8 3 per cent (SD) In an attempt to obtain as uniform sieves as possible the flow rate of filtered plasma through the different sieves was measured and only sieves with a flow rate that was less than ±4 per cent (range) were used The filters were re used after the following washing procedure After rinsing with tap water the sieves were placed in 10 per cent chromsulphuric acid rinsed in distilled water and dried between filter papers

Preparation of the blood samples Venous blood from healthy human subjects was obtained by venipuncture and anticoagulated with heparin (10 IU/ml) The blood was first centrifuged at 6 000 g for 10 min The buffy coat was removed from the red cells Any white cells and platelets were removed by the separation method of NAKAO et coll (1973) Thus 5 ml of wet sulphoethyl cellulosa (SEC Serva) and 10 ml of wet Sephadex 25 (Pharmacia) were mixed packed in a column 5 cm in diameter and equilibrated with a solution containing 0 138 M NaCl 0 005 M $MgCl_2$ 10 units ml⁻¹ of heparin and 0 01 M potassium phosphate buffer pH 7 5 Five ml of plasma or 2 5 ml of the red cells in a 0 154 M NaCl solution were added to the column which was then eluted with the NaCl $MgCl_2$ heparin mixture However as it is not known to what degree the plasma proteins are influenced by this separation method 10 per cent of the centrifugated plasma was filtered only through Millipore filters (type RA) with a nominal pore diameter of 1 2 μm The red cells were separated from the eluent by centrifugation and then mixed with the plasma The hematocrit was fixed to 10 per cent by removing erythrocytes

Red cells from each blood sample were checked by interference contrast micro-

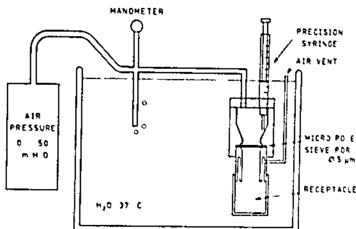


Fig 1 Schematic representation of the apparatus

rigidity of the red cell (CHIEN et coll 1967 SCHMID SCHÖNBEIN & WELLS 1973 SCHMID SCHÖNBEIN et coll 1969) caused by the hypertonic contrast media This rigidification of the red cell increases with increasing osmolality of the contrast medium

Whether this rigidification of the red cell also affects its ability to pass through the capillaries and whether there is any difference in this effect on cells exposed to contrast media of different osmolalities was the purpose of the present investigation This was done by measuring the ability of the red cell to pass through a dynamic and geometric model of the nutrient capillaries

Material and Methods

Principles of the method The flow times of 1 ml of a 10 per cent red cell suspension in plasma (V_1) and of 1 ml plasma (V_2) through Nucleopore sieves (nominal pore diameter 5 µm) are determined by a stopwatch The flow rate of each suspension and plasma is computed and the relative flow rate (V_{rel}) i e the flow rate of the red cell suspension divided by the flow rate of plasma is taken as a quantitative measurement of red cell deformability

The apparatus used is shown schematically in Fig 1 It has been described in detail by SCHMID SCHÖNBEIN et coll (1969) The sieve which has a diameter of 13 mm is firmly attached between two parts of the measuring chamber with help of a rubber seal ring (O ring) The upper part of the measuring chamber is sealed air tight and is connected to a large air reservoir (50 l) in which a constant air pressure (50 mm H_2O) is maintained and measured Introduction of a small volume (1 ml) of fluid from a calibrated syringe was made into the upper part The lower part of the measuring chamber consists of a teflon tube leading into an aerated receptable The whole unit is made of plexiglass with water thight fittings and can be inserted into a thermostated water tank (37°C) Six of this apparatus are assembled into one unit allowing

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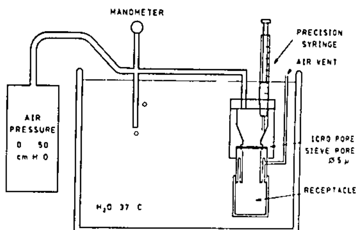


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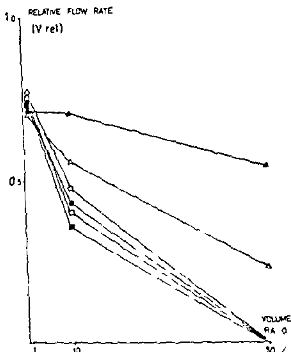


Fig 2 Effect on the deformability of the red blood cells by measuring the relative flow rate V_{rel} (V_{RBC} V_{plasma}) of 10 red blood cell suspensions in plasma mixed with contrast media and hypertonic saline at different volume ratios (test solution/10 RBC suspension) The cells were filtered through Nucleopore sieves of 5 μm in diameter ΔP = 50 mm H_2O Temperature 37 C ■ Isopaque Cerebral △ Amipaque 280 Dimer X ■ Urografin 60 ▲ Amipaque 170 ● NaCl (1 5 osm)

Results

The flow rates measured both of the 10 per cent red cell suspensions (V_1) and the plasma (V_2) appear in Table 2 The calculated relative flow rates ($V_{r\,l}$) are presented in Table 2 and graphically illustrated in Fig 2

Effects of contrast media on the flow rate of 10 per cent red cell suspension (V_1) All the contrast media and the hypertonic saline solution decreased the flow rate of the red cell suspension with increasing volume ratio (Table 2) At 50 per cent volume ratio the suspensions of the high osmotic ionic contrast media Isopaque Cerebral Urografin 60° and Dimer X and the hypertonic saline did not pass through the sieves

Effect of contrast media on the flow rate of plasma (V_2) All the contrast media solutions decreased the flow rate of plasma with increasing volume ratio while the hypertonic saline increased the flow rate with increasing volume ratio (Table 2)

Effect of contrast media on the relative flow rate (V_{rl}) (Fig 2) One per cent volume ratio No statistically significant difference was found between either the V_{rl} of the red cell suspension without additive (10 hct) and the red cell suspension mixed with contrast medium or between the different contrast media solutions ($p < 0\ 1$)

Table 2

Effect of contrast media on deformability of human red cells as measured by flow of 1 ml of a 10 RBC suspension (V_1) and 1 ml of plasma (V_2) through 5 μm Nucleopore sieves at 37 C Δp = 50 mm H_2O Values presented are mean values + SD n = 24

Test solution	Volume ratio test solution blood ( )	V_1 (μl/s)	V_2 (μl/s)	V_{rel} (V_1 V_2)
10 RBC in plasma		36±7	48±8	0 75±0 19
10 RBC in plasma + Amipaque	1	34±6	45±7	0 73±0 17
170 mg I/ml	10	29±5	40±7	0 71±0 18
	50	18±3	35±5	0 54±0 12
10 RBC in plasma + Amipaque	1	32±5	46±9	0 71±0 18
280 mg I/ml	10	19±4	34±5	0 56±0 13
	50	4±0 9	19±3	0 23±0 06
10 RBC in plasma + Dimer X	1	34±6	43±8	0 79±0 20
280 mg I/ml	10	16±4	35±6	0 48±0 14
	50	0	21±3	0
10 RBC in plasma + Isopaque	1	33±6	44±6	0 77±0 18
Cerebral 280 mg I/ml	10	15±4	36±6	0 41±0 12
	50	0	28±4	0
10 RBC in plasma + Urografin	1	35±7	46±7	0 76±0 19
60 290 mg I/ml	10	14±3	38±5	0 37±0 10
	50	0	26±3	0
10 RBC in plasma + NaCl	1	37±7	50±9	0 74±0 20
(1 5 osm)	10	24±4	56±10	0 43±0 10
	50	0	63±15	0

scopy and white cells and platelets were counted The red cells were all found to be smoothly disc shaped and behaved normally under shear No leucocytes and less than 1 000 thrombocytes/μl were found

In order to test to what degree different contrast media solutions influence red cell deformability plasma was removed and contrast medium was added to the samples The following volume ratios contrast medium to 10 per cent red cell suspension were prepared 1 10 and 50 per cent The following contrast media were investigated A Ionic monomeric Isopaque Cerebral (meglumine/calcium metrizoate) and Urografin 60 % (meglumine/sodium diatrizoate) B Ionic dimeric Dimer X (meglumine iocarmate) C Non ionic monomeric Amipaque (metrizamide) The iodine concentration osmolality and viscosity of the contrast media are presented in Table 1 Also the effect of hypertonic (1 5 osm) NaCl was investigated The statistical differences were calculated from Student s t test

BURTON (1966) and FUNG (1966) first postulated that the deformability of the red cell is dependent on three factors (1) The geometry of the cell (surface to volume relationship) (2) the internal structure of the membrane (the bending flexibility of the membrane) and (3) the fluidity of the cell content Hypertonic solutions of contrast media might influence the red cell in all these three regards Thus it has been demonstrated that due to the high osmolality of the contrast media solutions there is a shift of water from the inside to the outside of the cells causing a shrinkage of the cells and a decrease in their diameter (ASPELIN 1978 a BERNSTEIN et coll 1964 BRAASCH BRÅNEMARK et coll 1969 LASSER et coll 1962 MCINTOSH et coll 1967) This would per se increase the deformability by reducing the volume but keeping the surface area constant However the loss of internal water increases the internal viscosity of the cell (BRAASCH ERSLEV & ATWATER 1963) so that the total effect of hypertonic solutions is a decreased deformability of the red cell

Contrast media produce changes in the membrane structure of the red cell as well Thus it was demonstrated that contrast media were able to convert the cells into echinocytes (crenated cells) in solutions both iso and hypertonic to blood (ASPELIN 1978 a) In isotonic (0 3 osm) solution the non ionic Amipaque converted more cells into echinocytes than Isopaque Cerebral Urografin 60 ₒ and Dimer X However the present results show that the echinocytes produced by the isotonic Amipaque are considerably less rigid ($p < 0\,001$) than the echinocytes produced by the hypertonic contrast media solutions in 10 per cent volume ratio

Only ionic contrast media of high osmolality (Isopaque Cerebral Urografin 60 ° and Dimer X) in high volume ratio converted red cells into desiccocytes (osmotically shrunken cells) (ASPELIN 1978 a) These desiccocytes were found to be more rigid in the present investigation ($p < 0\,001$) than the echinocytes that were produced by the non ionic Amipaque 280

Thus although hypertonic contrast media solutions might influence all three factors that affect red cell deformability the present results indicate that the osmolality which influences mainly the internal viscosity of the cell is the most important in this regard

The finding that contrast media can rigidify the red cells to that extent that they cannot pass through pores of 5 μm in diameter in vitro is also in agreement with investigations in vivo BROWN et coll and MOORE et coll (1970) analysed the effect of ionic contrast media on the microcirculation of the small bowel in dogs with high speed cinemicrography They found that red cells in contact with the contrast media became crenated and that these crenated cells were unable to enter the capillaries and red cell flow in the capillaries almost ceased

This rigidification of the red cell is also the most likely explanation for the increase in pulmonary arterial pressure that follows the injection of hypertonic solutions into the right side of the heart (ASPELIN 1978 a BINET & BURSTEIN 1951 ELIAKIM et coll 1956 FRIESINGER et coll 1965 READ et coll 1959 1960 SEMLER et coll 1958) This increase in pressure is due to an increased resistance to blood flow through the

Ten per cent volume ratio At this level the V_{rel} of the red cell suspensions in plasma (0 75±0 19) were higher ($p<0\ 001$) than those of Amipaque 280 (0 56±0 13) Isopaque Cerebral (0 41±0 12) Urografin 60% (0 37±0 10) and Dimer X (0 48±0 14) No statistical difference ($p>0\ 1$) was found between the V_{rel} of the latter three contrast media but the V_{rel} of Amipaque 280 was higher than those of Urografin 60% ($p<0\ 001$) Isopaque Cerebral ($p<0\ 001$) and Dimer X ($p<0\ 005$)

Fifty per cent volume ratio The red cell suspensions of Isopaque Cerebral Urografin 60% and Dimer X were not able to pass through the sieves and the calculated V_{rel} was zero The V_{rel} of both the isotonic Amipaque 170 (0 54±0 12) and the hypertonic Amipaque 280 (0 23±0 06) were lower ($p<0\ 001$) compared with that of *the red cell suspension without additive* The V_{rel} of *Amipaque 170 was higher* ($p<0\ 001$) than that of Amipaque 280

Effect of hypertonic saline (1 5 osm) on the relative flow rate (V_{rel}) One per cent volume ratio The V_{rel} of the hypertonic saline solution (0 71±0 20) was not statistically different from either the red cell suspension in plasma or the different contrast media solutions ($p>0\ 2$)

Ten per cent volume ratio The V_{rel} of the hypertonic saline (0 43±0 1) was lower ($p<0\ 001$) compared with those of red cells in plasma the Amipaque 170 and Amipaque 280 but was not significantly different ($p>0\ 02$) to those of the ionic Isopaque Cerebral Urografin 60% and Dimer X

Fifty per cent volume ratio The red cell suspension mixed with the hypertonic saline was not able to pass through the sieves and the calculated V_{rel} was zero

Discussion

It is evident that both the hypertonic saline and the hypertonic contrast media decrease the flow rate of the 10 per cent red cell suspensions The flow rate of the plasma was also decreased by the hypertonic contrast media but was increased by *the hypertonic saline This indicates that the decrease in flow rate of the red cell* suspension is mainly an effect of the hypertonicity of the solution while the flow rate of plasma is dependent mainly on the viscosity of the solution

The V_{rel} of the 10 per cent red cell suspension without additive in the present series (0 75) is slightly higher than in that of SCHMID SCHÖNBEIN et coll (1973) (0 68) where the same apparatus was used This fact might be explained by the new separation method that was used in the present investigation By this separation fewer leucocytes and thrombocytes were present in the samples and will therefore to a lesser extent block the pores and reduce the flow rate (LINDGARD 1974 a b)

It is also obvious that the exposure of hypertonic contrast media to blood results in a decreased *deformability of the red cell to pass through pores of approximately* 5 μm in diameter It is also evident that the higher the osmolality of the contrast medium the more the deformability is reduced

BURTON (1966) and FUNG (1966) first postulated that the deformability of the red cell is dependent on three factors (1) The geometry of the cell (surface to volume relationship) (2) the internal structure of the membrane (the bending flexibility of the membrane) and (3) the fluidity of the cell content Hypertonic solutions of con trast media might influence the red cell in all these three regards Thus it has been demonstrated that due to the high osmolality of the contrast media solutions there is a shift of water from the inside to the outside of the cells causing a shrinkage of the cells and a decrease in their diameter (ASPELIN 1978 a BERNSTEIN et coll 1964 BRAASCH BRÅNEMARK et coll 1969 LASSER et coll 1962 MCINTOSH et coll 1967) This would per se increase the deformability by reducing the volume but keeping the surface area constant However the loss of internal water increases the internal viscosity of the cell (BRAASCH ERSLEV & ATWATER 1963) so that the total effect of hypertonic solutions is a decreased deformability of the red cell

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Effect of hypertonic saline (1 5 osm) on the relative flow rate (V_{rel}) One per cent volume ratio The V_{rel} of the hypertonic saline solution (0 71±0 20) was not statistically different from either the red cell suspension in plasma or the different contrast media solutions ($p>0\ 2$)

Ten per cent volume ratio The V_{rel} of the hypertonic saline (0 43±0 1) was lower ($p<0\ 001$) compared with those of red cells in plasma the Amipaque 170 and Amipaque 280 but was not significantly different ($p>0\ 02$) to those of the ionic Isopaque Cerebral Urografin 60% and Dimer X

Fifty per cent volume ratio The red cell suspension mixed with the hypertonic saline was not able to pass through the sieves and the calculated V_{rel} was zero

Discussion

It is evident that both the hypertonic saline and the hypertonic contrast media decrease the flow rate of the 10 per cent red cell suspensions The flow rate of the plasma was also decreased by the hypertonic contrast media but was increased by the hypertonic saline This indicates that the decrease in flow rate of the red cell suspension is mainly an effect of the hypertonicity of the solution while the flow rate of plasma is dependent mainly on the viscosity of the solution

The V_{rel} of the 10 per cent red cell suspension without additive in the present series (0 75) is slightly higher than in that of SCHMID SCHÖNBEIN et coll (1973) (0 68) where the same apparatus was used This fact might be explained by the new separation method that was used in the present investigation By this separation fewer leucocytes and thrombocytes were present in the samples and will therefore to a lesser extent block the pores and reduce the flow rate (LINDGARD 1974 a b)

It is also obvious that the exposure of hypertonic contrast media to blood results in a decreased deformability of the red cell to pass through pores of approximately 5 μm in diameter It is also evident that the higher the osmolality of the contrast medium the more the deformability is reduced

retardation of flow and less dilution are to be expected both effects which are favourable for demonstrating the veins Another possible method for obtaining a still shorter circulation time through the organ would be to wash out the red cells of the organ with an isotonic solution before injecting the contrast medium The latter will pass more rapidly through the organ since no crenated rigidified cells block the capillaries and thus the circulation This method has already been utilized to improve the demonstration of the mesenteric veins (HEPP et coll 1968) A further advantage of this method is that the toxicity of the contrast medium is reduced since the contact time contrast medium–organ is decreased

SUMMARY

The effect on red cell deformability from solutions of the ionic contrast media diatrizoate iocarmate and metrizoate and the non ionic metrizamide and hypertonic saline (1 5 osm) was investigated by measuring the flow rate of 10% red cell suspension (V_{RBC}) and of plasma (V_{plasma}) through Nucleopore sieves of 5 μm in diameter By calculating the relative flow rate V_{rel} (V_{RBC}/V_{plasma}) the deformability of the red cell was quantified Both the contrast media solutions and the hypertonic saline solution decreased the V_{rel} indicating an increased rigidity of the red cell The increased rigidity was due mainly to the osmotic effect The higher the osmolality the more the deformability was reduced The low osmotic metrizamide induced a smaller reduction in red cell deformability compared to ionic media of high osmolality in iodine-equivalent concentration

ZUSAMMENFASSUNG

Die Wirkung von Losungen der ionisierten Kontrastmittel Diatrizoat Iocarmat und Metrizoat und des nicht ionisierten Metrizamid sowie hypertonische Salzlosung (1,5 osm) auf die Deformierbarkeit der roten Blutzellen wurde durch Messungen der Flussgeschwindigkeit von 10% roten Blutzellsuspensionen (V_{RBZ}) und von Plasma (V_{Plasma}) durch Nucleopore Siebe 5 μm im Diameter untersucht Durch Berechnung der relativen Flussgeschwindigkeit V_{rel} (V_{RBZ}/V_{Plasma}) wurde die Deformierbarkeit der roten Blutzellen quantitativ bestimmt Sowohl die Kontrastmittellosungen als auch die hypertonische Salzlosung verminderten die V_{rel} was auf einen Anstieg der Rigidität der roten Blutzellen hindeutet Dieser Anstieg war hauptsachlich durch den osmotischen Effekt verursacht Je hoher die Osmolalitat je stärker war die Deformierbarkeit herabgesetzt Metrizamid mit niedriger Osmolalitat verursachte eine geringere Reduktion in der Deformierbarkeit der roten Blutzellen verglichen mit den ionisierten Mitteln mit hoher Osmolalitat in Jod-equivalenten Konzentrationen

RÉSUMÉ

L effet sur la deformabilite des globules rouges de solutions de moyen de contraste ionique diatrizoate iocarmate et métrizoate et du moyen de contraste non ionique métrizamide et de solution saline hypertonique (1 5 osm) a été étudié en mesurant la vitesse d ecoulement d une suspension de globules rouges à 10% (V_{GR}) et de plasma (V_{plasma}) à travers des filtres Nucleopores de 5 μm de diamètre En calculant le débit relatif V_{rel} (V_{GR}/V_{plasma}) la déformabilité du globule rouge a été quantifiee Les solutions de moyen de contraste ainsi que

pulmonary capillaries (READ et coll *1960)* These authors also demonstrated that the presence of the red cells is necessary to obtain this pressure change This increase in pressure was first believed to be caused by an increased red cell aggregation caused by the contrast media and that these aggregates were blocking the capillaries (READ et coll 1959, 1960) However it has been pointed out that both hypertonic solutions and contrast media solutions desaggregate the red cells (ASPELIN & SCHMID SCHÖNBEIN 1978 EHRLY & MÜLLER 1966 GERLACH & DEUTICKE 1966, READ et coll 1959, SCHMID SCHÖNBEIN et coll 1975) and therefore an increased resistance to flow through the capillaries occurs Nevertheless it should be stated that when the rigidified red cells block the capillaries the slowing of the flow stimulates the formation of red cell aggregates which thus secondarily further reduces the red cell flow through the capillaries

MIYAMOTO & MOLL (1971) demonstrated that the red cells have to deform in order to pass through the pulmonary capillaries This explanation that the rigidified red *cell might block the capillary and thus cause the increase in pulmonary arterial pres* sure is also supported by the findings of EFFROS (1972) Normally the red cell transit time through the lungs is shorter than that of plasma (DOW et coll 1972 ERSLEV & ATWATER) *However, EFFROS found in experiments in dogs that the injection of* hypertonic solutions into the jugular vein markedly decreased the red cell transit time which became much longer compared with the transit time of plasma that remained unchanged *He also considered that this decrease in transit time of the red* cells might be explained by the reduced deformability of the red cells and that they blocked the capillaries

The present finding that the low osmotic non ionic Amipaque and the dimer ionic Dimer X reduced the deformability of the red cells less than the high osmotic Isopaque Cerebral and Urografin 60 % is in agreement with the results of ALMÉN et coll and ALMÉN & ASPELIN The contrast media which they found to cause the least increase in pulmonary arterial pressure when injected into the right atrium or ventricle were the same as those which in the present investigation produced the least red cell rigidification

Consequently by using contrast media with low osmolality the disturbances in blood flow through the capillaries following the injection are less than if contrast media of high osmolality are used This effect is to be expected in all vascular regions However it may have the greatest importance in the pulmonary circulation where no dilatory effect of the contrast media on the peripheral vascular bed has been observed This effect on the microcirculation may also be useful in efforts to demonstrate the veins Therefore the use of contrast media with high iodine content and consequently high osmolality for better demonstration of the veins may have a negative effect The flow will be retarded due to the crenation and rigidification of the red cells and the dilution of the contrast media will be increased due to the osmolality of the solution By using media of low osmolality if possible isotonic to blood (Amipaque has at this osmolality an iodine concentration of *170 mg I/ml)* less

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la solution salée hypertonique diminuent le V_{rel} indiquant une augmentation de la rigidité du globule rouge L augmentation de la rigidité est due principalement à l effet osmotique Plus l osmolalité est élevée plus la déformabilité est réduite Le métrizamide qui a une faible osmolalité provoque une plus faible réduction de la déformabilité du globule rouge par comparaison avec les moyens de contraste ioniques de forte osmolalité pour une concentration en iode équivalente

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PROTEINURIA FOLLOWING NEPHROANGIOGRAPHY

IV Comparison in dogs between ionic and non ionic contrast media

S HOLTÅS and L TEJLER

A profound but transitory increase in glomerular permeability leading to massive proteinuria is frequent following nephroangiography in man (TEJLER et coll 1977 a) and dogs (HOLTÅS et coll 1978 a) with commonly used ionic monomeric contrast media Recent reports indicate that temporary decreased renal function following angiography is more common than currently realized (OLDER et coll 1976 KRUMLOVSKY et coll 1978) Increased glomerular leakage of plasma proteins might be one factor in the development of renal failure in some patients following nephroangiography (TEJLER et coll 1977 b)

Nephroangiography is performed nowadays in increasing frequency in patients with severely injured kidneys and also in patients with vulnerable transplanted kidneys A non diseased or essentially healthy kidney might tolerate and repair the injury caused by the contrast medium but there is probably a risk that severely diseased kidneys might develop permanent damage following angiography To reduce this risk it is important to find contrast media which interfere as little as possible with glomerular function

A comparison has been performed between the degree of albuminuria (glomerular dysfunction) following nephroangiography in dogs with the commonly used ionic contrast medium Urografin 76 % (diatrizoate) the non ionic Amipaque (metrizamide) and a non ionic contrast medium with the code name C 29 recently synthesized by Nyegaard & Co The results are now reported

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Table 2

Number of dogs in the experimental groups reacting with relative increases of urinary albumin exceeding 100 and 1 000 respectively

Group	No of dogs	Relative increase	
		>100	1 000
I	35	32	19
II	17	15	11
III	29	12	3

For this ratio the term relative increase of urinary albumin is used Differences were considered significant when p-values 0 05 were obtained by the Mann Whitney rank sum test

Results

Following nephroangiography relative increases of urinary albumin exceeding 1 000 were observed in 19 of the 35 dogs (frequency 0 54) receiving the ionic contrast medium Urografin 76 % in 11 of the 17 dogs (frequency 0 65) receiving the non ionic Amipaque and in 3 of the 29 dogs (frequency 0 10) receiving the non ionic C29 (Table 2)

The relative increases of urinary albumin following injection of C29 (median 49) were significantly lower than those following injection of Urografin 76 (median 1 300) and Amipaque (median 1 700 Table 3)

After injection of Urografin 76 % the concentration of urinary albumin reached 50 per cent of the plasma concentration in 17 of 35 dogs (frequency 0 49) after injection of Amipaque in 11 of 17 dogs (frequency 0 65) and after injection of C29 in 2 of 29 dogs (frequency 0 07 Table 4)

Discussion

Nephroangiography in man with the commonly used ionic contrast medium Isopaque (metrizoate) frequently causes a marked but transitory increase of glomerular permeability leading to proteinuria (TEJLER et coll 1977 a) In dogs it was shown that the proteinuria was caused by the contrast medium and not by the catheterization procedure and no difference was found in the degree of proteinuria after nephroangiography with Isopaque (metrizoate) or Urografin (diatrizoate) (HOLTÅS et coll 1978 a) In the present investigation the albuminuric effect of the non ionic contrast medium Amipaque (metrizamide) and a new non ionic contrast medium with the code name C29 was compared with that of Urografin 76 %

Table 1

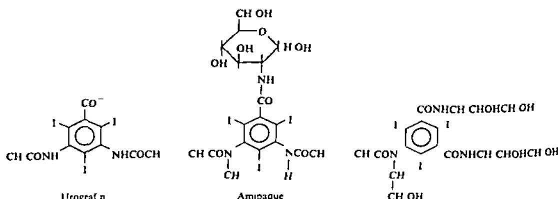
Number of dogs and dose osmolality and iodine content of the different contrast media injected selectively into one renal artery in the experimental groups

Group	No of dogs	Injected solution	Dose ml/20 kg	Osmolality Osm	Iodine content mol/l (mg ml)
I	35	Urografin 76	10	2 1	2 9 (370)
II	17	Amipaque	10	0 7	2 9 (370)
III	29	C29	10	0 7	2 9 (370)

Materials and Methods

The experiments were performed on mongrel dogs weighing on the average 21 kg (range 12–38 kg) anesthetized with intravenous Mebumal (pentobarbitone) and breathing spontaneously through an endothracheal tube Arterial and urinary bladder catheterizations were performed as previously described (HOLTAS et coll 1978 a) The dogs were divided into 3 groups The concentration of urinary albumin was determined following injection into one renal artery of the ionic contrast medium Urografin 76®, (group I) or the non ionic contrast media Amipaque (group II) and C 29 (group III) The number of dogs in the groups and dose osmolality and iodine content of the contrast media are given in Table 1

Structural formulas of the contrast media used



Urine samples were obtained via the transurethral catheter before and 15 30 and 60 min after the injection In all dogs one arterial blood sample was taken before the injection of the contrast medium Concentrations of albumin and creatinine in urine and plasma were determined as previously described and concentrations of urinary albumin were expressed per gram creatinine for reasons previously discussed (HOLTÅS et coll 1978 a) The ratio between the maximum post injection concentration of urinary albumin and the preinjection value was calculated for each animal

Table 4

Number of dogs in which urinary albumin concentration reached 50 and 100 per cent of the plasma concentration following angiography

Group	Total	No of dogs	
		Alb(urine)/Alb(plasma)	
		≥50	≥100
I	35	17	11
II	17	11	8
III	29	2	1

angiographic period For instance the risk of developing acute renal failure is probably enhanced after removal of a diseased kidney soon after nephroangiography leaving the patient with only one kidney which might have a defective glomerular function

However it is possible to reduce the glomerular dysfunction following nephroangiography by changing the chemical structure of the contrast medium as demonstrated by the significantly lower albuminuria produced by C29 than by Urografin 76 or Amipaque It is suggested that the present animal experimental model should be applied in the screening of new contrast media that are intended for nephroangiography so that media causing the least possible glomerular dysfunction (proteinuria) will be generally available

Acknowledgements

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SUMMARY

The degree of albuminuria following nephroangiography with the ionic contrast medium Urografin the non ionic Amipaque and a recently synthesized non ionic contrast medium with the code name C 29 was compared Significantly less albuminuria was caused by C 29 than by the other two contrast media

ZUSAMMENFASSUNG

Der Umfang der Albuminurie im Anschluss an einer Nephroangiographie mit dem ionisierten Kontrastmittel Urografin dem nicht ionisierten Amipaque und einem kurzlich

Table 3

Median and range of albumin concentrations in pre injection urine samples and in the post injection urine samples with maximum albumin concentration Median and range of the relative increases are also given Concentrations of albumin in urine are expressed in arbitrary units/g creatinine

Group	Conc of albumin in urine		Relative increase of urinary albumin
	Pre injection	Post injection	
I	0 44	570	1 300
	(0 092–2 6)	(9 5–3 500)	(20–21 900)
II	0 26	630	1 700
	(0 093–1 6)	(7 5–3 400)	(50–14 000)
III	0 80	30	49
	(0 069–2 6)	(1 6–2 200)	(1 6–32 000)

Statistical evaluation of differences between the groups (Mann Whitney) I–III and II–III $p<0\ 001$

Nephroangiography with C29 caused significantly lower relative increases of urinary albumin than Urografin 76% and Amipaque

It is obvious that high osmolality of the injected medium is not the main cause of the albuminuria since Urografin 76% with an osmolality of 2 1 Osm and Amipaque with an osmolality of 0 7 Osm did not differ in the degree of post angiographic albuminuria Furthermore C29 caused less albuminuria than Amipaque despite the fact that the two contrast media have about the same osmolality Thus, the chemical structure seems to be more important than the osmolality which is in accordance with the observations in previous experiments in which a hypertonic sodium chloride solution was compared with Urografin 76% (HOLTÅS et coll 1978 b) As has been observed both in man (TEJLER et coll 1977 a) and dog (HOLTÅS et coll 1978 a) individual factors probably also play an important role in the development of post angiographic albuminuria since in each group the degree of albuminuria varied widely following injection of the same contrast medium (Table 3)

In animal experiments Amipaque has a lower toxicity intravenously and in the subarachnoid space (SALVESEN 1973 a) causes less injury to aortic endothelium (ALMÉN et coll 1973) induces less cardiovascular effects (ALMÉN 1973 a b) and less injury to the blood brain barrier (SALVESEN 1973 b) than currently used ionic contrast media Although Amipaque has superior properties in many organs when compared with ionic contrast media the kidney seems to be an exception as evidenced by the present results and also from observations on the mitotic rate in rabbit tubular cells which did not differ after nephroangiography with Amipaque Dimer X (meglumine iocarmate) or Isopaque (metrizoate) (SKALPE & EVENSEN 1973)

It seems important to be aware of the glomerular dysfunction following nephro angiography and it is probably wise to avoid major surgery in the immediate post

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EXCRETION OF SODIUM AND METHYLGLUCAMINE DIATRIZOATE AFTER LONGTIME UNILATERAL URETERIC STASIS IN THE RABBIT

T OWMAN

Urography is a commonly used method for the examination of ureteric stasis and several clinical reports have appeared on this subject since urography was introduced in the 1930 s (BOEMINGHAUS 1932 HELLMER 1935 WULFF 1948) animal experiments have also been performed although much less extensively (WULFF ELKIN et coll 1964 BRENES et coll 1966 AMIGSTEIN et coll 1972 ELKIN 1975 GOLMAN et coll 1976) However a detailed analysis of the excretion after longtime unilateral ureteric occlusion has not been made previously

Material and Methods

The material comprised 32 rabbits each weighing 2 0 to 3 0 kg The animals were given general anaesthesia by pentobarbitone sodium (Mebumalnatrium ACO Sweden) intravenously Through a retroperitoneal approach the left ureter was ligated close to the lower pole of the kidney Penicillin was administered post operatively in a single large injection intramuscularly The rabbits were divided into two groups and one and two weeks later respectively the excretion of diatrizoate was examined in the following way The animals were given general anaesthesia as described and the right ureter was dissected free retroperitoneally ligated and cannulated with a baby feeding tube (3 5 F 1 15 mm Argyle England) A rubber band was

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synthetisierten nicht jonisierten Kontrastmittel mit dem Codenamen C 29 wurde verglichen Eine statistisch geringere Albuminurie wurde durch C 29 als durch die anderen beiden Kontrastmittel hervorgerufen

RÉSUME

Les auteurs ont comparé le degré d albuminurie après néphroangiographie faite avec le moyen de contraste ionique Urografin le moyen de contraste non ionique Amipaque et un *moyen de contraste non ionique récemment synthétisé portant le nom de code C 29* Le C 29 donne une albuminurie significativement moindre que les deux autres moyens de contraste

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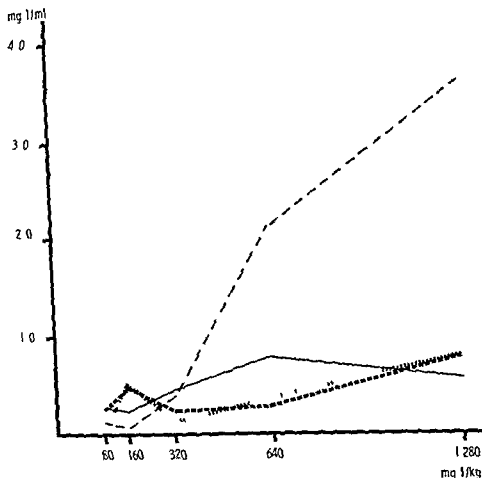
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Standard deviations ($\pm \bar{x}$)

	Dose				
	80	160	320	640	1 280
NaD 1 w	0 14	0 14	0 42	0 06	0 36
NaD 2 w	0 27	0 45	0 14	0 23	0 11
MeD 1 w	0 01	0 03	0 22	1 70	2 60
MeD 2 w	0 01	0 51	0 11	0 23	0 51

Fig 1 Iodine concentration (mg I/ml) in urine of the stasis kidney following one or two weeks stasis 2 h after intravenous injection (mg I/kg b w) of sodium diatrizoate (—— 1 w —— 2 w) and meglumine diatrizoate (- - - 1 w 2 w) At one week the meglumine salt yields a higher concentration than the sodium salt Standard deviations are very large at dose levels 640 and 1 280 mg I/kg b w (MeD 1 w)

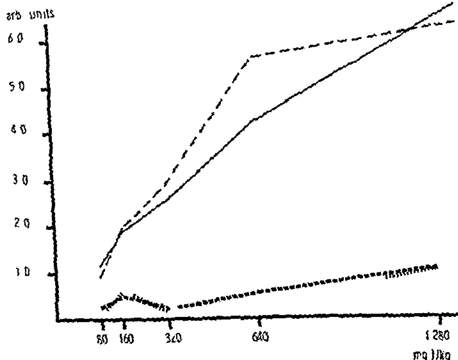
tied around the ureter and tube to prevent leakage of urine A superficial artery and a vein were also cannulated The body temperature was kept constant at 37 0 to 37 5 C using a heating pad An injection consisting of sodium or methylglucamine diatrizoate was then given intravenously as a bolus in doses of 80 160 320, 640, and 1 280 mg I/kg body weight The diatrizoate salts were labelled with ^{125}I or ^{131}I for convenient analysis in a scintillation detector (Selektronik, Denmark) Urine from the right ureter was sampled in 12 min periods, and volume and iodine concentration were measured No ureteral compression was applied Blood analysis for iodine concentration was made in the middle of each period of urine sampling The excretion was interrupted after two hours, when the animals were killed The kidneys were removed and weighed The pelvis of the left kidney was opened and the amount of urine and its iodine concentration measured The renal parenchyma of both kidneys was then minced using an Ultra Thurrax (Janke & Kunkel West Germany) and the iodine concentration analysed

Results

The iodine concentration of the urine from the occluded side increased with the dosage of diatrizoate salt administered (Fig 1) The sodium salt had the same iodine concentration in the urine after one as after two weeks of urinary occlusion but meglumine salt reached a much higher concentration up to 3 5 mg I/ml urine after one week of urinary occlusion However, when standard deviations were calculated large deviations were found for the meglumine salt (one week occlusion) and the level of urine concentration at the higher doses may well give a false impression After two weeks of urinary stasis it was slightly below 1 mg I/ml urine at the highest dose level (1 280 mg I/kg b w) The type of salt sodium or methylglucamine had no significant effect on the iodine concentration in the urine Probably no real difference exists between the two salts and the duration of ureteral occlusion

The attenuation produced by a urographic contrast medium is a function not only of the iodine concentration but also of the thickness of the layer of contrast containing urine The product of iodine concentration and layer thickness i e the estimated attenuation capacity is the adequate measure from the radiographic point of view The approximate thickness of the layer can be estimated as the third root of the volume of the renal pelvis and the parenchyma respectively (OWMAN & OLIN 1979) The estimated attenuation of the renal parenchyma and the pelvis after one and two weeks of ureteral occlusion are given in Figs 2 and 3 After one week of occlusion the sodium salt in the renal pelvis seemed to give a lower attenuation than did the meglumine salt The attenuation of the parenchyma however was equivalent for the two salts Although the standard deviations are fairly large it is obvious that parenchymal attenuation was higher than the pelvic one for both salts after both one and two weeks of occlusion

The iodine concentration of the parenchyma of the intact kidney and the stasis kidney is demonstrated in Fig 4 The concentration increased with the dose in-



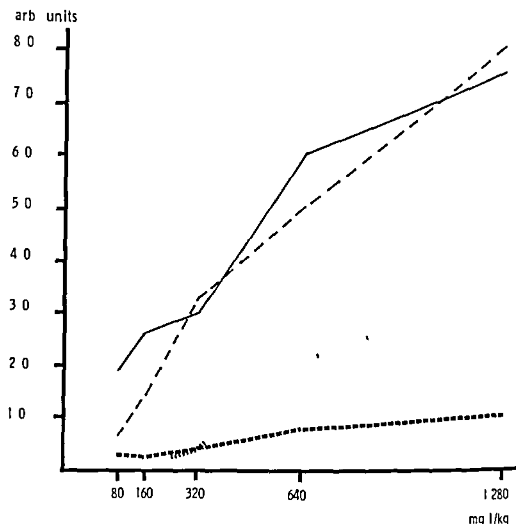
Standard deviations (±s)

	Dose				
	80	160	320	640	1 280
NaD par	0 63	0 43	2 14	2 74	2.14
NaD urine	0 27	0 45	0 14	0 23	0 11
MeD par	0 88	0 96	0 21	2 10	1 38
MeD urine	0 01	0 28	0 06	0 23	0 51

Fig 3 Estimated attenuation (arb units) of renal pelvis and parenchyma of the obstructed kidney following two week s stasis and 2 h after intravenous injection (mg I/kg b w) of sodium diatrizoate (—— urine —— parenchyma) or meglumine diatrizoate (urine —— parenchyma) Less attenuation of renal pelvis than of parenchyma independent of type of salt

dependent of the type of salt No difference seemed to exist due to the two salts or the time of ureteral occlusion Urinary concentrations reached similar levels on the two sides Blood iodine concentration increased with increasing dose and no difference due to type of salt or duration of occlusion was noted (Fig 5)

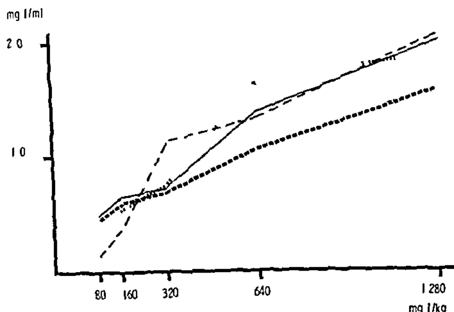
The vascular volume of the kidney is approximately 50 per cent of the total volume (LYRDAL & OLIN 1975) and since the blood concentration of iodine is known it is



Standard deviations ($\pm \bar{x}$)

	Dose				
	80	160	320	640	1 280
NaD par	0 81	1 99	1 97	2 07	2 04
NaD urine	0 14	0 14	0 42	0 06	0 36
MeD par	0 14	0 30	0 01	0 56	2 40
MeD urine	0 01	0 03	0 22	1 70	2 60

Fig 2 Estimated attenuation (arb units) of renal pelvis and parenchyma of the obstructed kidney following one week s stasis and 2 h after intra venous injection (mg I/kg b w) of sodium diatrizoate (—— urine —— parenchyma) or meglumine diatrizoate (urine --- parenchyma) Attenuation of parenchyma is higher than that of renal pelvis Probably no real difference between sodium and meglumine salt in renal pelvic attenuation

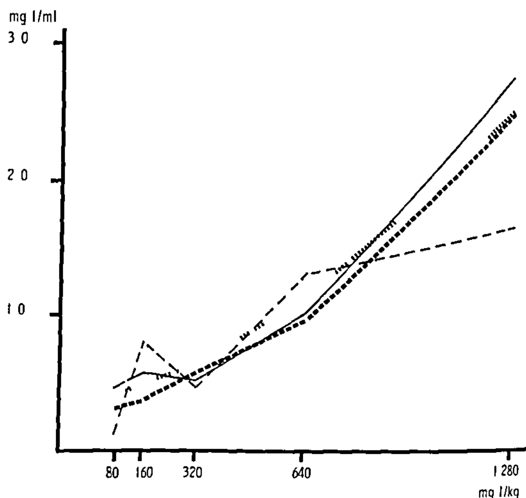


Standard deviations (± *x*)

	Dose				
	80	160	320	640	1 280
NaD 1 w	0 18	0 46	0 58	0 35	0 07
NaD 2 w	0 13	0 06	0 20	0 55	0 68
MeD 1 w	0 04	0 09	0 52	0 52	0 71
MeD 2 w	0 14	0 30	0 06	0 82	0 65

Fig 4 Iodine concentration of renal parenchyma following contra lateral stasis of one and two weeks duration and after intravenous in jection (mg I/kg b w) of sodium diatrizoate (—— 1 w —— 2 w) or meglumine diatrizoate (—— 1 w ---- 2 w) Concentration produced is independent of type of salt Left Intact kidney Right Stasis kidney

is made certain differences are revealed In Fig 7 the excretion rate of iodine following the injection of contrast medium at a dose of 320 *mg I/kg* body weight is given for animals with free urine flow (bilateral excretion) and for animals in which unilateral ureteric occlusion had been instituted for one and two weeks respectively (intact kidney) During the first period after the intravenous injection when the blood concentration of iodine was high e g about 0 60 *mg I/ml at 24* min the excretion rate was higher for animals with intact kidneys than for animals who had one or two weeks of ureteric obstruction In the concentration range 0 60 to 0 30 mg I/ml

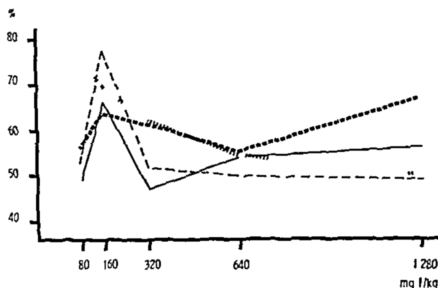


Standard deviations ($\pm \bar{x}$)

	Dose				
	80	160	320	640	1 280
NaD 1 w	0 49	0 27	0 14	0 21	1 73
NaD 2 w	0 22	0 18	0 17	0 35	1 20
MeD 1 w	0 01	0 69	0 06	0 41	0 38
MeD 2 w	0 16	0 25	0 30	0 40	1 37

Fig 4 (For legend see opposite page)

possible to calculate the amount of iodine contained in the kidney vessels In the intact kidney the vascular part was 12 % ± 3 of the iodine contained in the kidney The amount of contrast medium administered which is excreted through the intact kidney for two hours averaged 58 per cent apparently regardless of type of salt or duration of occlusion (Fig 6) The highest excretion rate was recorded at a dose of 160 mg I/kg body weight However if a detailed analysis of the course of excretion



Standard deviations (±s)

	Dose				
	80	160	320	640	1 280
NaD 1 w	24 7	11 6	0	0 7	6 4
NaD 2 w	7 7	14.2	13 4	8 9	12 0
MeD 1 w	1 4	12.7	3 5	8.5	3 5
MeD 2 w	2.8	21 2	12.0	7 1	10 6

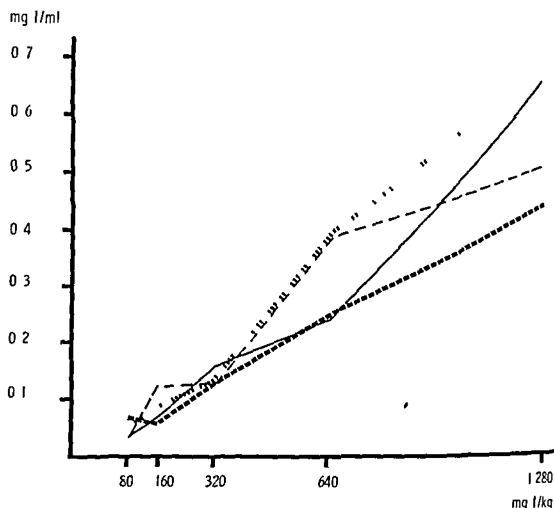
Fig. 6 Excretion in per cent of administered dose from non-obstructed kidney during a 2 h period following intravenous injection (mg I/kg b w) of sodium diatrizoate (—— 1 w ------ 2 w) or meglumine diatrizoate (---- 1 w 2 w) Mean excretion after one or two weeks stasis is 58±9 1 per cent

groups of animals The weight of the intact kidney was 8 9±1 6 g after one week of contralateral ureteric stasis and 10 5±1 4 g after two weeks of ureteric stasis (no adjustment for body weight)

Discussion

Two hours after the administration of contrast medium the renal parenchyma i e the tubular system usually revealed higher attenuation than did the renal pelvis (Figs 3 4) in the animals subjected to one or two weeks of unilateral ureteric obstruction This corresponds clinically to the nephrographic phase occurring at urography during urinary stasis

The mechanism behind the nephrographic phase during urography has been open



Standard deviations (± σ)

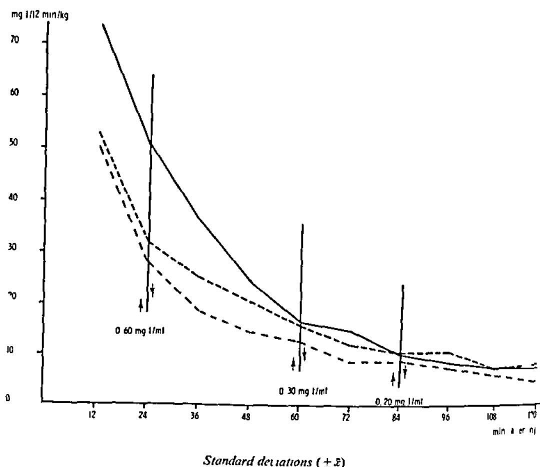
	Dose				
	80	160	320	640	1 280
NaD 1 w	0 01	0 02	0 05	0 04	0 11
NaD 2 w	0 06	0 02	0 01	0 12	0 09
MeD 1 w	0 01	0 07	0 03	0 04	0 17
MeD 2 w	0 01	0 03	0 04	0 16	0 33

Fig 5 Iodine concentration (mg I/ml) in blood 2 h after intravenous injection (mg I/kg b w) of sodium diatrizoate (—— 1 w – — 2 w) or meglumine diatrizoate (–·– 1 w 2 w) No difference between type of salt or duration of stasis

blood the excretion rate for animals after two weeks of urinary stasis approached that for animals with intact kidneys at low blood concentrations Not until concentrations dropped below 0 20 mg I/ml blood were animals who had one week of urinary occlusion capable of an excretion rate of the same order as that of the other

artery and Miokon (sodium diprotrizoate) in the other could demonstrate that most of the nephrographic effect was due to accumulation of the contrast medium in the tubular lumina rather than in the blood vessels Also using Thorotrast CHAMBERLAIN & SHERWOOD (1967) could similarly exclude contrast medium in the vascular compartment as a significant feature of the nephrographic effect Uptake of contrast media in the tubular cells may also contribute to the nephrography but in vitro this has not been not confirmed (SHERWOOD et coll 1967 MUDGE et coll 1971) although AMIGSTEIN et coll occasionally found diatrizoate in rat tubular cells after ureteral occlusion Some tubular excretion of contrast media has been reported (DENNEBERG 1965 DONALDSON 1968 MUDGE et coll GOLMAN et coll) and although this would amount only to one to two per cent it may be of importance in ureteral stasis However ELKIN after blocking tubular excretion using probenecide in animals with urinary stasis still obtained good nephrographic effect Accumulation of contrast medium in the interstitial compartment was denied by AMIGSTEIN et coll and seems unlikely unless there is tubular injury Thus it is most likely that the obstruction nephrography is due mainly to contrast medium excreted through glomerular filtration and accumulated in the lumina of dilated tubules (HARROW & SLOANE 1965 BRENES et coll KOROBKIN et coll 1971 SHERWOOD 1971 FRY & CATTELL 1972 AMIGSTEIN et coll ELKIN)

Continuous glomerular filtration even after longtime ureteral blockage has been reported In the initial stages it seems to be due mainly to dilatation of the collecting duct system with increasing impairment of glomerular filtration upon increasing intratubular pressure The rise in tubular pressure will be higher in a state of diuresis (ELKIN et coll) After maximum intratubular intrapelvic pressure has been reached, glomerular filtration will continue at a low level but never ceases (MALVIN et coll 1958 OMACHI & MACEY 1959 TAYLOR & ULLMANN 1961 SALOMON & LANZA 1962 SELKURT 1963 SUKI et coll 1971 NABER & MADSEN 1973 a CLAUSEN & HOPE 1977) This seems mainly to be due to active reabsorption of sodium and other solutes along the nephron obligating further reabsorption of water (ELKIN et coll) With increasing pressure the intraluminar fluid will also find alternate ways out of the collecting system either by pyelolymphatic or by pyelovenous backflow (SALOMON & LANZA ELKIN et coll NABER & MADSEN 1973 a b) According to NABER & MADSEN (1973 b) in dog experiments all examined substances up to the molecular size of colloids possibly also bacteria are absorbed via lymph or blood vessels Whether the reabsorption is due to mucosal rifts or to the opening of preformed channels was not concluded Thus it seems possible that contrast media can also be absorbed via these routes It is not clear whether the lymphatic or the venous route is the more important but NABER & MADSEN (1973 a) who found only approximately 0 3 per cent of renal hilar lymph flow to represent urine absorbed from the renal pelvis concluded that the pyelohaematogenous pathway was the more efficient Leakage of urine to perirenal tissue through calyceal or pelvic ruptures may also occur and this has probably happened in several instances as a gelatinous mass was fairly often



Standard deviations ($\pm \bar{x}$)

	Time									
	12	24	36	48	60	72	84	96	108	120
1 w	3 8	6 2	6 1	7 4	2 3	1 8	1 5	0 8	0 8	0 5
2 w	4 2	3 9	6 6	6 7	2 3	1 4	1 1	0 9	0 2	0 5
N	7 1	2 9	4 3	4 1	4 1	7 4	3 2	1 2	0 9	0 7

Fig 7 Excretion of iodine in free urine flow following intravenous injection 320 mg I/kg b w Normal bilateral excretion in 2 animals (——) excretion in intact kidney in 2 with contralateral stasis for one week (---) and in 2 with stasis for two weeks (– –) At high iodine concentrations of blood (> 0 60 mg I/ml) excretion is more efficient in normal animals than in animals with stasis In concentrations from 0 60 to 0 30 mg I/ml elimination in animals with two weeks stasis is approaching normal At low concentrations (< 0 20 mg I/ml) elimination is approximately equivalent in all categories

to some debate EDLING et coll (1957) by blocking tubular excretion with PAH in the rabbit found no nephrographic effect after the injection of Umbradil and concluded that the nephrography normally obtained with this contrast medium was due to its accumulation in the tubular cells Later EDLING & HELANDER (1959) by injecting Thorotrast (which is not to any extent excreted by the kidney) in one renal

SUMMARY

The excretion of sodium and meglumine diatrizoate was examined following one or two weeks of unilateral ureteric occlusion No difference between the two diatrizoate salts was found. A slow compensatory increase of the function of the intact kidney occurred but after two weeks it was still insufficient at high blood con~entration levels

ZUSAMMENFASSUNG

Die Ausscheidung von Natrium und Meglumin Diatrizoat wurde nach einer unilateralen Okklusion des Ureters wahrend einer oder zwei Wochen unter ucht Kein Unterschied zwischen den beiden Diatrizoat Salzen wurde gefunden Ein langsammer kompensatorischer Anstieg der Funktion der intakten Niere erfolgte dieser war jedoch noch nach zwei Wochen bei hohen Blutkonzentrationsspiegeln ungenugend

RÉSUMÉ

L excrétion du diatrizoate de sodium et de méglumine a éte étudiee après une ou deux semaines d occlusion uretérale unilaterale L auteur n a pas trouve de différence entre les deux sels de diatrizoate Une lente augmentation compensatoire de la fonction du rein intact apparait mais au bout de deux semaines elle est encore insuffisante pour des niveaux de concentration sanguine éleves

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found surrounding the kidney and ureter This could also explain the rather wide variation in results in some cases

In the present experiments a higher attenuation was found in the renal parenchyma of the stasis kidney than in the stasis urine after both one and two weeks of ureteral occlusion This must be due to the small amount of contrast medium filtered by the glomerulae and the very slow passage of urine down the tubules into the renal pelvis The difference in attenuation possibly would have decreased if a longer observation period had been applied No difference between the two salts was found this could not be expected as the possible filtration of the sodium and meglumine ions would be too small to be of any consequence to water and solute reabsorption or intratubular intrapelvic pressure

A detailed analysis of the excretion of the contrast medium administered in a dose of 320 mg I/kg body weight revealed that the intact kidney had an insufficient excretion capacity at high blood concentrations of medium At intermediate blood concentrations (0 30 mg I/ml) which were reached about one hour after the injection the intact kidney had a good compensatory excretion capacity where contralateral ureteric occlusion had been applied for two weeks Not until a blood concentration of 0 20 mg I/ml had been reached (84 min) was a good compensatory excretion capacity noted in cases where contralateral ureteric occlusion had been applied for only one week The compensatory increase in function of the intact kidney starts immediately (DICKER & SHIRLEY 1971, LYRDAL & OLIN) but, nevertheless after two weeks of contralateral ureteric obstruction it was still insufficient at high blood concentrations of contrast media

The increase in function of the intact kidney is also reflected in the weight of the kidney After two weeks of urinary occlusion the intact kidney was 1 6 g heavier than after one week of occlusion suggesting some degree of compensatory hyperplasia Ample evidence of compensatory renal growth after unilateral nephrectomy has been reported (ANDERSON 1967 COE & KORTY 1967 MALT 1969 DICKER & SHIRLEY LYRDAL & OLIN MOGENSEN et coll 1977) but not so after unilateral ureteral obstruction However PAULSON & FRALEY (1973) found compensatory growth through both hypertrophy and hyperplasia after ureteral ligation in mice and concluded that the stimulus for accelerated renal growth was the functional rather than the physical removal of renal mass

The amount of contrast medium excreted by the intact kidney in two hours represents slightly more than 50 per cent of the injected dose In a rabbit with two normal kidneys this amount is excreted in about one hour This fact also illustrates that the intact kidney cannot produce a complete functional compensation after contralateral ureteric stasis of only one or two weeks duration The excretion capacity after one or two weeks of contralateral urinary occlusion was the same for sodium as for meglumine diatrizoate

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VOLUME OF DISTRIBUTION OF CONTRAST MEDIA IN BLOOD

M KORMANO

Until recently the volume of distribution of contrast media in tissues has been of little interest due to the absence of its diagnostic application After an intravascular injection the concentration of the contrast medium rapidly diminishes due to mixing with blood and leakage into the extravascular space (KORMANO & DEAN 1976 DEAN & KORMANO 1977 a b) Since intravascular media do not normally penetrate the *red blood cells* (RBC) (LANGECKER et coll 1954 PHELPS et coll 1973) the distribution volume in blood should equal 100 minus hematocrit (HCT) percentage *grossly* independent of the amount of contrast medium Subsequent increase in the distribution volume is caused by extravascular distribution (DEAN & KORMANO 1977 a b NEWHOUSE 1977 DEAN et coll to be published) The increase of roentgen attenuation of blood and tissues caused by contrast medium injection can be detected by computer tomography and has been used empirically in CT diagnosis since its introduction (AMBROSE 1973)

From experimental evidence the idea of using distribution volume as an additional aid in CT diagnosis was introduced by DEAN et coll (1978 a) based on the equation

$$\text{distribution volume of tissue} = (100 - \text{HCT}\%) \times \frac{\text{contrast enhancement of tissue}}{\text{contrast enhancement of blood}}$$

While the contrast enhancement can be estimated merely by viewing the CT images and more accurately measured by subtraction (BERGSTRÖM & SUNDMAN 1976 ZILKHA

Submitted for publication 23 January 1978

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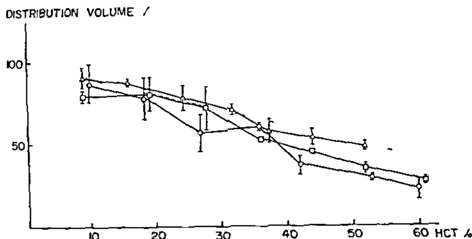


Fig 2 Distribution volume of iodipamide in blood in relation to hematocrit ○ = 2 mM □ = 10 mM △ = 50 mM — = expected mean

HCT value and contrast concentration The measured activity/ml allowed calculation of the volume of distribution of activity in each mixture and its correlation to the individual HCT measurements

Results

In preliminary experiments using the HCT sample supernatant for measuring activity widely varying usually erroneously large distribution volumes were obtained probably due to uneven distribution of heavy contrast molecules after centrifugation It was therefore necessary to measure the activity from well mixed uncentrifuged samples of reconstructed whole blood at varying hematocrit levels

The results with varying concentration of meglumine diatrizoate appear in Fig 1 and with meglumine iodipamide in Fig 2 Allowing for the variation due to inaccuracy of the measurements distribution volumes showed values as expected and a good linear correlation to HCT value below 40 per cent in all concentrations The lowest (2 mM) concentration of diatrizoate and the two lower concentration levels of iodipamide gave distribution volumes 10 to 20 per cent lower than expected in all HCT values exceeding 40 per cent

Discussion

The blood concentrations obtained after an intravenous injection of 100 ml of 10 per cent diatrizoate for contrast enhancement will increase the attenuation coefficient of blood by an average of 45 Hounsfield units (22 5 EMI units) with considerable variation (GADO et coll 1975) This represents an iodine concentration of about 2 mg/ml as estimated from the data of HINDMARSH (1975) and GADO et coll Thus

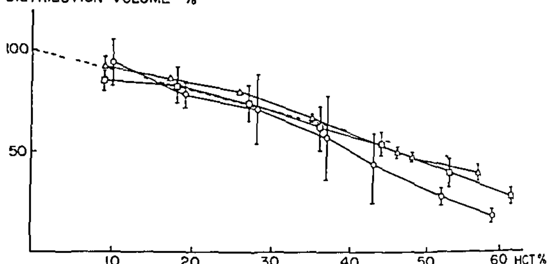


Fig 1 Distribution volume of diatrizoate in blood in relation to hematocrit ○ = 2 mM □ = 10 mM △ = 50 mM - expected mean

et coll 1976) the distribution volume of individual tissues is not readily visibl but can be obtained with simple calculations from the above equation Statistical treat ment of experimental results shows that measurement of distribution volume charge with time provides new diagnostic information on tissues (DEAN et coll 1978)

The accuracy of such measurements is dependent on the factors related to th CT scanner as far as the attenuation readings are concerned and to the reliability of the estimated blood distribution volume based on HCT per cent To provide data for the estimation of the validity of this approach the volume of distribution of two commonly used ionic contrast media in blood was determined in relation to HCT per cent and contrast concentration

Materials and Methods

Venous blood from healthy human subjects was anticoagulated with citrate blood cells and plasma separated by centrifugation Non labeled 60 % meglumine diatrizoate (Angiografin Schering AG Berlin) and 17 % meglumine iodipamide (Biligrafin Schering AG Berlin) were mixed with small amounts of the same 10 % ¹²⁵I label d compounds Contrast mixtures were added to plasma to make final concentrations of 50 mM 10 mM and 2 mM Red blood cells were then returned to plasma in quantities required to produce varying hematocrit values from 10 to 60 per cent samples without blood cells serving as a reference The resulting suspension samples 6 0 ml each were incubated in 37 C for 10 min with continuous shaking Triplicate 100 μl suspension samples diluted with 900 μl of saline were used for activity measure ments The true final HCT of the mixture was measured from double 100 μl samples by the microhematocrit method Four separate experiments were carried out for each

ZUSAMMENFASSUNG

Die Volumenverteilung von Diatrizoat und Iodipamid im Blut in Relation zum Hämatokrit und zur Kontrastkonzentration wurde unter Verwendung von [125]I gezeichneten Substanzen gemessen. Bei Konzentrationen die nach intravenöser Injektion auftraten war das prozentuelle Volumen der Distribution bei beiden Kontrastmitteln 100 minus Hämatokrit mit Ausnahme für hohe Hämatokritwerte welche zu einer ungleichmässigen Verteilung der Kontrastmittel bei geringen Konzentrationen führen können. Kein Hinweis auf eine intrazelluläre Penetration wurde erhalten.

RÉSUMÉ

Le volume de distribution du diatrizoate et de l'iodipamide dans le sang par rapport à l'hématocrite et à la concentration du moyen de contraste a été mesuré en utilisant des composés marqués au I. Aux concentrations obtenues après injection intraveineuse le pourcentage du volume de distribution de ces deux moyens de contraste est 100 hématocrite excepté pour les hautes valeurs de l'hématocrite qui peuvent donner une distribution inégal des moyens de contraste aux plus faibles concentrations. Il n'y a pas eu de preuve de la pénétration intracellulaire des moyens de contraste.

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the two lower diatrizoate concentrations represent the average upper and lower limits of contrast concentration reached in clinical contrast enhancement It appears that for the purpose of calculating contrast distribution volume of a given tissue from CT scans with the help of HCT and contrast enhancement of a cross section of a major blood vessel like the aorta or vena cava no appreciable error will be caused by the assumption that the distribution volume percentage in blood equals 100 minus HCT, at least in HCT values below 40 per cent

Contrast media decrease HCT in vitro by osmotic shrinkage of the red blood cells (ASPELIN 1976) A temporary decrease of HCT also occurs in vivo with an arterial dose of 3 ml/kg (AMIEL et coll 1977) As the true value of capillary HCT in tissue cannot be measured these two factors will inevitably introduce an error to the estimated distribution volume of blood and hence to the calculated distribution volume of tissue

The extravascular component is significantly greater in the case of tissue enhancement (KORMANO & DEAN NEWHOUSE DEAN et coll to be published) in most tissues The rapidity of expansion of the contrast distribution volume with time in individual tissues may have more diagnostic value than a single measurement (DEAN et coll 1978 to be published) Thus a possible error in the estimate of blood distribution volume will not abolish the diagnostic potential of consecutive distribution volume measurements

BERNSTEIN et coll (1964) observed a change in the packing characteristics of red blood cells with small concentrations of iodipamide but not so with diatrizoate Toxic influences unrelated to osmotic effect also introduce increased deformability of red blood cells (ASPELIN) Osmotic and toxic deformation of these cells may improve the distribution of the contrast molecules around cell walls and into the aggregates while low concentrations may distribute unevenly among closely packed red blood cells Such influences may have caused smaller distribution volumes of contrast media with high hematocrit values Whether this is true also in patients with polycythemia remains to be established In agreement with previous investigations (LANGECKER et coll PHELPS et coll) there was no evidence of intracellular distribution of either diatrizoate or iodipamide

Acknowledgements

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SUMMARY

The volume of distribution of diatrizoate and iodipamide in blood in relation to hematocrit and contrast concentration was measured using ^{125}I labeled compounds In concentration obtained after intravenous injection the percentage volume of distribution of both contrast media is 100 minus hematocrit except for high hematocrit values which may cause uneven distribution of contrast media in smaller concentrations No evidence of intracellular penetration was obtained

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METRIZAMIDE IN HIGH-DOSE UROGRAPHY

A KOLBENSTVEDT E ANDREW B CHRISTOPHERSEN K GOLMAN
B KVARSTEIN and H H LIEN

The use of the non ionic water soluble contrast medium metrizamide (Amipaque) has been widely accepted for subarachnoid application due to its toxicologic and radiologic properties (LINDGREN 1977) Less attention has been focused on the use of metrizamide in angiography and urography The general toxicity of metrizamide in animals is lower than that of ionic contrast media (SALVESEN 1973 a b) while no difference in local toxicity was found after selective injection into the renal artery (SKALPE & EVENSEN 1973) In experimental urography (ALMÉN et coll 1973 GOLMAN & ALMÉN 1976 EVILL & BENNESS 1977) the iodine concentration in the urine was higher at certain dose levels of metrizamide than with corresponding doses of ordinary ionic contrast media

Metrizamide has been used clinically in angiographic examinations with signi ficantly less subjective reactions and less influence on haemodynamic parameters than with ionic media (ALMEN et coll 1977 ENGE et coll 1977 SKALPE et coll 1977 SKJENNALD 1978 ALBRECHTSSON & OLSSON 1979) Urography in 9 human adults performed with 40 ml metrizamide 300 mg I/ml caused no adverse reaction or signs of toxicity based on a large number of laboratory data from samples of blood and urine (ALMÉN et coll personal communication) A higher iodine concentration in the renal pelvis after metrizamide injection than after injection of ordinary ionic contrast media was indicated GOLMAN et coll (1977) found in man that most of the intravenously injected metrizamide was excreted through the kidneys and that renal tubular reabsorption of metrizamide occurred

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Table 1

Effect of high-dose metrizamide urography on laboratory blood data (tests without significant changes excluded)

	Immediately before injection		5 min after injection		24 h after injection		72 h after injection	
	Median	Range	Median	Range	Median	Range	Median	Range
Na mmol l	139	135–140	13	134–137	139	135–141	138	137–143
Ca mmol/l	2 3	2 3–2 4	2 2*	2 1–2 4	2 4	2 2–2 4	2 3	2 2–2 4
Total protein g l	69	65–80	65	59–70	71	64–73	70	66–74
ASAT U/l	[illegible]	10–35	13	9–22	17	12–31	18	10–35
LD U/l	616	170–1 160	252	133–640	298	220–1 040	330	148–1 130
T_3-test	1 03	0 91–1 12	0 95	0 89–1 07	1 02	0 89–1 10	1 05	0 88–1 08

Statistically significant $p \leq 0.05$

than after a previous low dose urography with a conventional ionic contrast medium

The high viscosity of the medium in the present concentration was considered a minor disadvantage at manual injection

No significant effect was noted on blood pressure or pulse rate

A statistically significant decrease in blood Na Ca total protein ASAT LD and T_3 test was observed in the samples taken 5 min after injection (Table 1) but not later The other blood tests demonstrated no significant changes

No significant changes occurred in the pooled 24 h post urographic urine A statistically significant rise in the excretion of Na Cl and P was found in pooled urine 48 to 72 h after injection (Table 2) The other urine parameters were not significantly changed

Discussion

In phlebographic (ALBRECHTSSON & OLSSON) and urographic (ALMÉN et coll personal communication) investigations metrizamide caused less adverse reactions than monomeric ionic contrast media In the present series high doses of metrizamide injected intravenously resulted in few subjective reactions and the sensation of heat appeared to be less for the patients who had previous experience of urography with ionic media However the limited number of patients does not allow any definite conclusion The absence of effect on a large number of laboratory tests after the high dose of metrizamide supports the conclusions drawn in previous animal and clinical investigations that the substance is at least as well tolerated as the ionic media

A transient 3 to 9 per cent decrease in concentration of Na Ca total protein and T_3 test was observed in the blood samples taken 5 min after injection This is probably

The low toxicity of metrizamide with few adverse reactions and possible improvement of the urographic information prompted the present investigation in order to evaluate the safety possible influence on laboratory parameters and the quality of the films following high doses of metrizamide in a group of patients with normal renal function

Materials and Methods

Urography was performed in 11 patients 5 males and 6 females aged 32 to 71 years using metrizamide 350 mg I/ml in a dose of 0 5 g I per kg body weight The injection rate was approximately 30 ml per min The volume ranged from 75 to 122 ml All patients had normal serum creatinine values They were admitted because of benign diseases of the urinary tract such as calculi ureteric obstruction recurrent infections or hyperplasia of the prostate The day before the examination the patients were on a *fluid diet* without milk and laxatives (Cascara Salax Ferring) were given as recommended by ROSENGREN & ÅBERG (1975) Films were exposed at 5 15 30 and 60 min after the injection of the contrast medium in an antecubital vein Abdominal compression was not applied Adverse reactions were recorded by questioning the patients Blood pressure and pulse rate were recorded before immediately after and 1 hour after injection

The following blood laboratory data were recorded immediately before the injection of contrast medium *as well as 5 min 24 h and 72 h after the injection* Erythrocyte sedimentation rate (ESR) leucocytes erythrocytes thrombocytes haemoglobin (Hb) osmolality Na K Cl Ca P urea creatinine total protein aspartate aminotransferase (ASAT) gamma glutamyl transpeptidase (GT) lactic dehydrogenase (LD) haptoglobin bilirubin uric acid thyroxine thyroid stimulating hormone (TSH) triiodothyronine (T_3) and triiodothyronine test (T_3 test)

The following urine laboratory data were recorded in pooled 24 h urine before *urography pooled 24 h urine after urography and pooled urine 48 to 72 h after urography* Na K Cl P creatinine urea alkaline phosphatase (aphos) β microglobulin and albumin

Statistical evaluation of the data was made by the Wilcoxon test for pair differences and the t test for paired observations (p 0 05 was considered significant)

Results

The quality of the films was good in all patients In one patient a film exposed 5 h after injection demonstrated contrast medium in the gall bladder as is also often seen at urography with ionic media

Nausea vomiting or urticaria did not occur Seven patients noticed a slight sensation of heat lasting from 1 to 5 min Urography with an ionic medium had previously been performed in 4 patients in all the sensation of heat was less prominent after the metrizamide injection One patient experienced a transient dizziness although less

Table 1

Effect of high-dose metrizamide urography on laboratory blood data (tests without significant changes excluded)

	Immediately before injection		5 min after injection		24 h after injection		72 h after injection	
	Median	Range	Median	Range	Median	Range	Median	Range
Na mmol/l	139	135–140	135*	134–137	139	135–141	138	137–143
Ca mmol/l	2.3	2.3–2.4	2.2	2.1–2.4	2.4	2.2–2.4	2.3	2.2–2.4
Total protein g/l	69	65–80	65	59–70	71	64–73	70	66–74
ASAT U/l	26	10–35	13*	9–22	17	12–31	18	10–35
LD U/l	616	170–1 160	25[illegible]	133–640	298	220–1 040	330	148–1 130
T_3-test	1.03	0.91–1.12	0.95*	0.89–1.07	1.02	0.89–1.10	1.05	0.88–1.08

* Statistically significant $p \leq 0.05$

than after a previous low-dose urography with a conventional ionic contrast medium.

The high viscosity of the medium in the present concentration was considered a minor disadvantage at manual injection.

No significant effect was noted on blood pressure or pulse rate.

A statistically significant decrease in blood Na, Ca, total protein, ASAT, LD and T_3 test was observed in the samples taken 5 min after injection (Table 1), but not later. The other blood tests demonstrated no significant changes.

No significant changes occurred in the pooled 24 h post urographic urine. A statistically significant rise in the excretion of Na, Cl and P was found in pooled urine 48 to 72 h after injection (Table 2). The other urine parameters were not significantly changed.

Discussion

In phlebographic (ALBRECHTSSON & OLSSON) and urographic (ALMÉN et coll. personal communication) investigations metrizamide caused less adverse reactions than monomeric ionic contrast media. In the present series high doses of metrizamide injected intravenously resulted in few subjective reactions and the sensation of heat appeared to be less for the patients who had previous experience of urography with ionic media. However, the limited number of patients does not allow any definite conclusion. The absence of effect on a large number of laboratory tests after the high dose of metrizamide supports the conclusions drawn in previous animal and clinical investigations that the substance is at least as well tolerated as the ionic media.

A transient 3 to 9 per cent decrease in concentration of Na, Ca, total protein and T_3 test was observed in the blood samples taken 5 min after injection. This is probably

Table 2

Effect of high dose metrizamide urography on laboratory urine data (tests without significant changes excluded)

Test	Pooled urine 24 h before urography		Pooled urine 24 h after urography		Pooled urine 48-72 h after urography	
	Median	Range	Median	Range	Median	Range
Na/creatinine mmol/mmol	8 47	3 52–11 90	7 70	5 43–15 90	11 20	6 76–20 90
Cl/creatinine mmol/mmol	8 20	2 27–11 60	8 07	3 94–17 40	11 20*	5 63–22 20
P/creatinine mmol/mmol	1 82	0 82–2 84	1 86	0 39–2 63	2 43*	0 95–3 14

* Statistically significant $p \leq 0\ 05$

due both to the dilution effect by the injected solution (approximately 4 % of total serum volume) and to the osmotic properties of the injected medium which will result in a transport of water from the extravascular space into the serum compartment Injection of ionic media where the osmotic effect is expected to be even greater, has been demonstrated to cause a decrease in Na Ca P and K in the order of 10 to 20 per cent of preinjection values when given in doses three times as high as those used in the present series (HAYEK et coll 1975 SHELDON & FUCHS 1977 AMIEL et coll 1977) The decrease in ionic concentration of the blood in the latter reports may also be attributed to blood dilution as AMIEL et coll found that the blood volume increased 15 to 20 per cent during the first 10 min after the injection of methylglucamine iothalamate

Apart from the T_3 test no thyroid function test (Thyroxine TSH and T_3) was significantly affected by the metrizamide injection These thyroid function tests therefore appear to be applicable as early as 24 h after injection of metrizamide contrary to the previously widely used iodide uptake test which was affected for several weeks after injection of iodine containing contrast media (TENG & KARAMOURTJOUNIS 1960 HAYASHI 1971)

The decrease in concentration of the enzymes LD and ASAT 5 min after injection is too great to be explained solely by the haemodilution In adults LD values in the interval 227 to 452 U/l are considered normal The preinjection median value (616 U/l) in the present material therefore seems to be abnormally high and the possibility of haemolysis in some of these samples has to be taken into consideration The concentration of ASAT is not as sensitive to haemolysis as the LD values and haemolysis is therefore not considered an explanation for the observed fall in the concentration of ASAT However, any toxic effect of the contrast medium would have been expected to increase and not to decrease the level of ASAT

In the urine all laboratory data have been related to the urine concentration of creatinine to obtain a more relevant statement for their excretion Previously an increase in the alkaline phosphatase and albumin excretion after intravenous injection of ionic and non ionic contrast media in doses of 370 to 700 mg I/kg to rabbit and dog was reported (HOLTÅS et coll 1978 GOLMAN to be published) This was not reproduced in the present series where only an insignificant increase in both variables was found However in the dog series of HOLTÅS et coll the urine was sampled the first posturographic hour and this interval is regarded as the period for maximum proteinuria

The increase in the excretion of Na Cl and P 48 to 72 h after the injection is probably not related to the contrast medium itself as 94 per cent of the dose is expected to leave the body within the first 24 h (GOLMAN et coll) More likely the late increase in Na Cl and P excretion is due to the prohibition of milk and the saline laxative given before the examination This diet would lower the excretion of these ions and when normal diet is re-established an increase in ion excretion would be expected A stress reaction with an increase of adrenal corticosteroids would have caused a retention of blood Na with a corresponding decrease of urinary excretion during the days following the examination It is thus unlikely that the late increase of urinary Na excretion in the present series is caused by a stress reaction

In this series the radiographic quality was in all cases evaluated as good Experiments in animals (GOLMAN & ALMÉN EVILL & BENNESS) and urographic results in man (ALMÉN et coll personal communication) have indicated that improved radiographic quality could be obtained using metrizamide relative to the ionic media However the number of patients in the present investigation was too limited to give any conclusive statement on this point

Conclusion

A high dose of metrizamide was well tolerated and the quality of the urographic films was good The few changes observed in the laboratory data were *regarded as clinically* unimportant and mainly produced by haemodilution As this dilution effect will be less prominent with the low osmotic medium relative to the ionic contrast media the use of metrizamide in high-dose urography is *recommended*

SUMMARY

The non ionic water soluble contrast medium metrizamide (Amipaque) was used for high dose urography in 11 patients with apparently normal renal function Films of good quality were obtained Adverse *reactions* and the effect on pulse and blood pressure as well as a large number of blood and *urine laboratory* parameters were recorded Only clinically insignificant effects occurred and the medium is recommended for further use in urography

ZUSAMMENFASSUNG

Das nicht ionisierte wasserlosliche Kontrastmittel Metrizamid (Amipaque) wurde fur die Hoch Dosis Urographie bei 11 Patienten mit offenbar normaler Nierenfunktion verwendet Filme von guter Qualitat wurden erhalten Nebenwirkungen und der Effekt auf Puls und Blutdruck sowie auf eine grosse Anzahl von Blut und Urin Parametern wurden untersucht Nur klinisch unbedeutende Effekte traten auf und das Mittel wird fur den weiteren Gebrauch bei der Urographie empfohlen

RESUMÉ

Le moyen de contraste hydrosoluble non ionique métrizamide (Amipaque) a été utilisé pour des urographies à forte dose chez 11 sujets ayant apparemment une fonction rénale normale On a obtenu des films de bonne qualité Les auteurs ont noté les effets secondaires et l effet sur le pouls et la pression artérielle ainsi qu un grand nombre de paramètres biologiques concernant le sang et l urine Il n y a eu que des effets cliniques insignifiants et ce moyen de contraste est recommandé pour etre utilisé en urographie

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THROMBOSIS FOLLOWING PHLEBOGRAPHY WITH IONIC AND NON-IONIC CONTRAST MEDIA

U ALBRECHTSSON and C G OLSSON

Increased ^{125}I fibrinogen uptake after normal phlebography was reported by HARRIS et coll (1975) and POULOSE et coll (1976) ALBRECHTSSON & OLSSON (1976) found such an increase after phlebography of the lower limb in as many as one third of the patients To elucidate the role of the osmolality of the contrast medium a randomized investigation was designed comparing media with different osmolality—meglumine-metrizoate and metrizamide

Material and Methods

The series constitutes part of a comparison between various methods to diagnose deep venous thrombosis Twenty one consecutive out patients with possible lower limb thrombosis were selected all with a normal ^{125}I fibrinogen uptake test at two measurements performed before phlebography The contrast medium used for phlebography was randomized and known only to the radiologist

The fibrinogen uptake was performed as described by NEGUS et coll (1968) with some modifications (OLSSON to be published) Following the intravenous injection of 100 μCi ^{125}I fibrinogen (Radiochemical Centre Amersham England) 5 measuring sequences were performed in each patient during 7 days At each sequence 12 adjacent corresponding points were measured in both legs The activity at each measuring point was expressed as percentage of the activity over the heart A uni directional

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percentage side difference in 3 or more adjacent points of at least 5-4-4 or 4-5-4 was considered abnormal (modified after BROWSE et coll 1971)

For phlebography of the lower limb the method of GREITZ (1954) was employed modified as later described by RABINOV & PAULIN (1972) The patient was placed on a tilting table at an angle of 45 to 65 to the horizontal plane The leg under examination did not bear weight and the patient was instructed to keep calf muscles relaxed Contrast medium was injected through a plastic cannula in a dorsal foot vein preferably that of the first toe In 9 patients a tourniquet at the ankle was used during part of the examination to improve filling of the fibular and posterior tibial veins or to avoid extensive filling of large varicose veins The contrast medium was inj cted in portions of 20 to 30 ml during fluoroscopy The total mean volumes were 88 ml (range 65–120) of meglumine-metrizoate and 74 ml (range 50–90) of metriza mide both with a concentration of 280 mg I/ml Exposures were made with an over head tube in a p lateral and oblique projections of the lower leg and a p and lateral of the femoral vein Films were also taken of the iliac vein during returning the table to horizontal and afterwards In two patients the femoral vein was injected to im prove filling of the iliac vein Rinsing the cannula with 20 ml of saline 0 9 concluded the examination The presence of an intraluminal filling defect outlined by contrast medium and seen in at least 2 films in different projections was the minimum require ment for the diagnosis of recent venous thrombosis Non filling of the deep veins was considered to indicate recent venous thrombosis only if an intraluminal defect was seen in at least one site Indirect signs such as non filling of veins or collateral flow were recorded as abnormal but not sufficient for the diagnosis of acute venous thrombosis

The contrast media used were Isopaque Cerebral and Amipaque (Nyegaard & Co Oslo Norway) Isopaque Cerebral (meglumine/calcium metrizoate 280 mg I/ml) is an ionic contrast medium with a high osmolality 1 46 mol/kg water Amipaque (metrizamide 280 mg I/ml) is a non ionic compound with an osmolality of 0 46 The osmolality of human serum is normally about 0 30

Results

Meglumine-metrizoate was used in 10 patients and metrizamide in 11 Of the 10 patients examined with meglumine-metrizoate 4 had small fresh thrombi at phlebo graphy In the remaining 6 patients the [1] I fibrinogen test turned positive after phlebography In 2 of these patients a second phlebography now with metrizamide demonstrated fresh thrombi in the foot and lower half of the calf especially the posterior tibial veins (Fig 1) In a third patient repeat phlebography with metri zamide did not reveal thrombus but distorted and narrowed veins especially in the foot (Fig 2) Three patients refused repeat phlebography

One of the 11 patients initially examined with metrizamide had a thrombosis at the first examination The remaining 10 patients had a normal [12] I fibrinogen uptake



Fig 1 Phlebography of the left lower leg a b) A p and c d) lateral projections No pathology at initial examination (a c) 3 days later (b d) thrombi in the posterior tibial veins (→)

in the leg except for one patient who had an elevated fibrinogen uptake over a visible hematoma after a puncture of the femoral vein

Immediate side effects such as urticaria pain nausea metallic taste and sensation of warmth were registered by the radiologist The most common complaint was an unpleasant feeling in the calf during and after injection of contrast medium There was a marked difference between the two contrast media in this respect most of the patients examined with meglumine-metrizoate complained spontaneously while the patients examined with metrizamide had none or slight discomfort Side effects such as nausea, sensation of warmth and metallic taste were also less frequent in the metrizamide group

The 3 patients who were subject to repeat phlebography with metrizamide 3 to 5 days after the first examination found the experience with meglumine-metrizoate unpleasant or very unpleasant compared to that with metrizamide

The delayed side effects were rather uniform consisting of pain and increased swelling of the foot and calf They appeared 2 to 10 hours after the procedure with meglumine-metrizoate and were accompanied by an abnormal ^{125}I fibrinogen uptake None of the patients exposed to metrizamide had such a reaction The symptoms and abnormal fibrinogen uptake following phlebography in the patients examined



Fig a) Normal appearance b) 4 days later small irregular vessels partly poorly filled no definite thrombus

with meglumine–metrizoate indicate a post phlebographic thrombosis or thrombophlebitis in the foot and calf The difference between the groups is statistically significant at the 0 2 per cent level according to Fisher s exact test The use of a tourniquet in 2 of the patients in the meglumine–metrizoate group and in 7 in the metrizamide group did not seem to influence the complication rate

The image quality was the same with the two contrast media although the amount of medium was somewhat less with metrizamide than with meglumine–metrizoate The explanation for this is probably that lower osmolality causes less dilution of the contrast medium

No correlation was found in the meglumine-metrizoate group between amount of medium used and the side effects and the small difference in amount of medium between the two groups cannot explain the difference in complication rate

Discussion

Phlebography of the lower limb is a reliable method for the diagnosis of deep venous thrombosis even when the lesions are small Side effects of phlebography have generally been considered unusual and mild probably depending on inadequate follow up However CRANLEY (1975) found fresh clots in the veins in 50 per cent of the patients operated upon the day after the phlebography HARRIS et coll found clinical signs and fibrinogen uptake indicating a post phlebographic thrombosis in 5 per cent of a series of patients with hip replacement During a survey of diagnostic tests of deep venous thrombosis (ALBRECHTSSON & OLSSON) an increased fibrinogen uptake was found after a normal phlebography in 33 per cent of cases BETTMANN & PAULIN (1977) found clinical signs of thrombophlebitis after phlebography in 3[illegible] per cent of unselected patients without initial thrombus a rate of complication which was reduced to 12 per cent on dilution of the contrast medium from 60 to 45 per cent In the reports quoted meglumine-amidotrizoate or meglumine-metrizoate was used as contrast medium

Infusion of dextrose water or saline with heparin through the catheter after phlebography has been used in order to reduce the risk of post phlebographic thrombosis (CRANLEY HARRIS et coll BETTMANN & PAULIN) however without evidence of a reduced rate of post phlebographic thrombosis

Administration of contrast medium has been demonstrated to decrease coagulation activity in vivo (BJÖRK 1968 STEIN & HILGARTNER 1968) ZIR et coll (1974) suggested that the contrast medium may also be a potent inhibitor of platelet aggregation and of platelet release

ZINNER & GOTTLOB (1959) MERSEREAU & ROCKE ROBERTSON (1961) and RITCHIE et coll (1974) have reported morphologic abnormalities in vessel endothelium after the administration of ionic contrast medium and glucose solution more severe with higher concentration of the solutions They were similar to those found in venous thrombosis ALMÉN et coll (1973) demonstrated that metrizamide produces less changes in the rat aortic endothelium than commonly used ionic contrast media of the same concentration

These findings indicate that the symptoms and the accumulation of ^{125}I fibrinogen probably indicate inflammatory reaction in the vessel wall with a secondary thrombus formation primarily caused by the high osmolality of the contrast medium

As a consequence isotope methods especially the ^{125}I fibrinogen test should be employed as the first diagnostic measure when deep venous thrombosis is suggested This test is sensitive when normal it excludes clinically significant deep venous thrombosis since an abnormal uptake may be caused by hematoma inflammation

or thrombus phlebography is still necessary for differentiation between these lesions to avoid undue anticoagulant therapy

Metrizamide is expensive but the cost is greatly exceeded by the cost for treatment of post phlebographic thrombosis and post thrombotic disease

The irritating side effects encountered with other contrast media seem to be absent when metrizamide is used and non ionic compounds of this type are recommended for routine use in phlebography

SUMMARY

The side-effects at phlebography of the lower limb were evaluated using an ionic contrast medium meglumine-metrizoate and a non ionic contrast medium metrizamide A post phlebographic accumulation of I fibrinogen was found in 6 patients examined with meglumine-metrizoate indicating a post phlebographic thrombosis Ten patients were examined with metrizamide with no post phlebographic increase in ^{125}I fibrinogen uptake Though the groups are small the difference is statistically significant at the 0 2 per cent level

ZUSAMMENFASSUNG

Die Nebeneffekte der Phlebographie des Beines unter Verwandung eines jonisierten Kontrastmittels Meglumin-Metrizoat und eines nicht jonisierten Mittels *Metrizamid* wurden festgestellt Eine Akkumulation von [12] I Fibrinogen nach der Phlebographie wurde bei 6 Patienten die mit Meglumin-Metrizoat untersucht worden waren gefunden was auf *eine Thrombose* hindeutet Zehn Patienten die mit Metrizamid untersucht worden waren wiesen keinen Anstieg in der I Fibrinogen Aufnahme nach der *Phlebographie auf Obwohl* die Gruppen klein sind sind die Differenzen auf dem 0 2 Prozent Niveau statistisch signifikant

RESUMÉ

Les effets secondaires de la phlébographie des membres inferieurs ont été évalués quand on utilise un moyen de contraste ionique le méglumine-metrizoate et un moyen de contraste non ionique le métrizamide Une fixation de *fibrinogène marquee au* [1] [5]*I* a ete constatée après la phlébographie chez 6 malades examines par le méglumine-métrizoate indiquant une thrombose post *phlébographique Dix malades* ont eté examines par le metrizamide sans augmentation après la phlébographie de la fixation du fibrinogène marqué a [1] I Bien que les groupes soient petits la différence est *statistiquement significative* au niveau de 0 2

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ENDOSCOPIC RETROGRADE DUCTOGRAPHY IN ADVANCED PANCREATITIS

Comparison between ERCP, angiography, surgery and microscopy of the pancreas

T SVAHN N GABRIELSSON I LJUNGDAHL and T THORGEIRSSON

Endoscopic retrograde cholangiopancreaticography (ERCP) has developed rapidly since McCUNE et coll (1968) performed the first endoscopic cannulation of the papilla and injected contrast medium into the pancreatic duct During the following years ERCP developed into a routine method chiefly due to achievements of Japanese gastroenterologists among others OI et coll (1970) Large *materials* have been collected concerning both the biliary tract (BLUMGART et coll 1972 SAFRANY et coll 1973) and disorders of the pancreas (ANACKER et coll 1972 CLASSEN et coll 1972 ZIMMON et coll 1974) However correlation of endoscopic *pancreato*graphy with results of surgery and microscopy has only been reported to a limited extent (HOWARD & NEDWICH 1971 ARNESJÖ *et coll 1974*)

The results of ERCP surgery microscopy and to some extent angiography in chronic pancreatitis of severe degree were compared and are now reported

Material

The material consisted of 16 patients 14 men and 2 women examined with ERCP and later operated upon The average age was 42 6 years with a range of 26 to 54 years

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Fig 1 a) Two concretions in pancreas b) Ductography reveals that one is located in the main duct and the other in a side branch (→)

The indication for the ERCP was in almost every case a history of chronic or relapsing pancreatitis in most of them ascribed to over consumption of ethyl alcohol

The ERCPs were performed with a duodenoscope with side optic Olympus JF B2 After cannulation of the papilla of Vater the ductal system of the pancreas was filled with water soluble contrast medium (Isopaque Cerebral Nyegaard Oslo) and films were exposed in several projections Attempts were made not to over distend the duct and prevent filling of the parenchyma

Selective coeliac angiography was carried out in 10 cases in 5 of these it was combined with angiography of the superior mesenteric artery in one with splenic portography and in one with percutaneous transhepatic portography The coeliac angiography was performed to assess the splenic vein and any collateral pathways No vasoactive drugs were used

Partial resection of the pancreas was performed in 12 cases in 9 of these the resection comprised only the tail of the gland In one case the intervention also in volved resection of the body in another both the body and a portion of the head of the pancreas In the remaining patient the head and body of the gland were resected In addition pancreatico jejunostomy was performed in 9 cases and choledocho jejunostomy in 2 cases Splenectomy was carried out in 10 patients Marsupialisation of a pancreatic cyst was performed in one case In another patient papillotomy was carried out and one of two ductal concretions diagnosed at the ERCP was removed (Fig 1) Surgery was limited to explorative laparotomy in 2 cases

The inflammatory lesion of the parenchyma was assessed on microscopy of resected specimens in 12 cases in direct connection with the operation In another case the preparation of the resected specimen failed and microscopy was impossible In one case the specimen was obtained by needle biopsy during operation in another

case only part of an extirpated cyst wall with adjacent parenchyma could be examined In the remaining case the severity of inflammation was evaluated at autopsy performed 3 months postoperatively

Methods

The radiologic criteria based on ERCP were mainly those presented by KASUGAI et coll (1972) for estimating the degree of pancreatitis Thus cases without obvious abnormalities were classified as belonging to group I Group II consisted of the cases with slight abnormalities of the side branches of the main duct Group III included cases with deformed side branches and slight abnormalities of the main duct (Fig 2) i e small lumen variations and also those cases in which the common bile duct was involved in the inflammatory process To group IV were referred cases with a highly irregular ductal system with stenotic and dilated segments concretions and cysts (Figs 3 4)

Since it was difficult to apply an identical classification of the inflammatory lesions present at angiography surgery and microscopy the grouping of the observations made with these methods was restricted to 3 grades

Thus at angiography group I comprised cases without vascular abnormalities while instances with slightly irregular appearances of the vessels were referred to group II Severe lesions in the arterial and venous vascularity with displaced stenotic or occluded intra or extrapancreatic vessels were assembled in group III

Similarly abnormal appearance of the pancreas at surgery was classified as *group I* while a moderately abnormal consistency on palpation of the gland and slight extra pancreatic inflammatory abnormalities were characteristic of *group II* *Group III* included cases with a marked increase in volume and consistency of the pancreas Cases with cysts thrombosis of the splenic vein or appreciable postinflammatory adhesions were also referred to this group

At microscopy normal cases were classified as belonging to group I Mild inflammatory lesions of the parenchyma were assigned to group II Fibrosis and considerable inflammatory abnormalities including necrosis and cysts were characteristic of cases belonging to group III

Results

At ERCP 15 of 16 patients were referred to group IV one to group III The assessment was based on observations made in those parts of the pancreas which revealed the most severe abnormalities and which were resected at the operation and also in most cases examined by microscopy

Seven of 10 cases examined with angiography were considered to belong to group III In the remaining 3 cases no abnormality was demonstrated at angiography

At surgery 2 of 16 cases were classified as belonging to group II while the remaining 14 cases were referred to group III



Fig 2 Moderately irregular main duct and branches suggestive of pancreatitis grade III



Fig 3 Contrast filled cyst and irregular main duct in caudal part of pancreas



Fig 4 Numerous concretions prevent complete filling of the extremely irregular main duct and branches

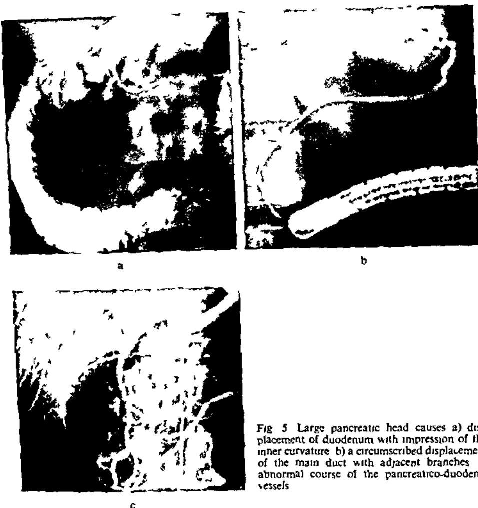


Fig 5 Large pancreatic head causes a) dis placement of duodenum with impression of the inner curvature b) a circumscribed displacement of the main duct with adjacent branches c) abnormal course of the pancreatico-duodenal vessels

On microscopy of the resected specimens or biopsies 14 cases could be assessed while one specimen could not be classified In a second case a needle biopsy only permitted the statement that malignant cells were not present in the specimen but that the material was too scanty to allow grading of the inflammation Of 14 operative specimens one was classified as belonging to group II 13 to group III

The results were in complete accordance in 4 cases with all four types of examination all belonging to the groups with the most severe inflammatory lesions

In 6 patients no angiography had been performed but according to the other three methods 5 cases were classified as indicating a severe degree of pancreatitis In 3 other cases no angiographic abnormality was observed although ERCP surgery and microscopy all characterized the inflammatory abnormalities as serious

In 2 cases microscopy was unfeasible but estimation in the other three respects agreed on advanced pancreatitis

A slight discrepancy was present in one case, surgery and microscopy indicated lesions characteristic of group II while the ERCP was typical of group III No angiography had been performed

In another case microscopy indicated group III and at duodenography, ERCP and angiography the enlarged pancreas made an impression into the wide duodenal loop associated with a circumscribed displacement of the pancreatic ductal system and pancreatico duodenal vessels (Fig 5) The extensive displacement of the duodenum and ducts was considered to be caused by a large cyst and the abnormality was therefore regarded as severe At operation one month later only a moderate increase in the consistency of the parenchyma was noted, and no cyst was found The surgical grading placed the case in group II

Discussion

For estimating the results of the ERCP the most severely injured parts of the pancreas were used for comparison The corresponding portions of the gland were resected at surgery The findings at ERCP angiography and operation thus became directly comparable at microscopy However at surgery and angiography even the peripancreatic lesions were included in assessing the degree of severity of the pancreatitis

On comparison between the findings at ERCP and at surgery the severity of the inflammatory lesions agreed well in 15/16 cases The operative findings were confirmed in 14 cases at microscopy of the resected specimens This evaluation of the stage of the pancreatitis also agreed well with the observations made at ERCP Only in one case was there a discrepancy of grouping angiography and duodenography demonstrated a lesion typical of a cyst which was not found at operation one month later This might be due to the cyst having emptied spontaneously in the interval between the examinations and operation and consequently was not palpable at surgery

Of the 10 cases examined with angiography complete agreement with ERCP concerning the stage of the inflammation was present in 7 The difficulty of assessing the result of angiography was demonstrated by the fact that no pathologic vascular abnormalities were evident in 3 cases although the inflammatory lesions observed at ERCP surgery and microscopy were considered to indicate the most severe grade of pancreatitis This is in keeping with experiences from other authors indicating that the angiographic appearances of chronic pancreatitis may be highly variable and sensitive to the technique of the examination (RÖSCH & BRET 1965 RANNIGER & SALDINO 1966 REUTER et coll 1969, BOIJSEN & TYLEN 1972 GÖTHLIN et coll 1974 MARIONS 1974)

It is true that the present angiographies were performed without resort to vasoactive

drugs and that this might have contributed to the less rewarding results Admittedly the material is small and the observations at the ERCP may have influenced the indications for surgery to comprise cases of serious pancreatitis only However a very strong impression nevertheless has been obtained regarding the capabilities of ERCP to present a detailed view of the extension and type of the abnormal morphology of chronic pancreatitis The findings were in good accordance with those encountered at surgery and microscopy Since a direct demonstration of the pancreatic ductal system is obtained at ERCP this method offers a considerably better means of information concerning the abnormalities of the parenchyma than does angiography (BOIJSEN & WEHLIN 1973) It is evident that partly different aspects of the nature of the disease are revealed at the various types of examination Thus for example important supplementary information on the peripancreatic extension of the inflammatory process and its influence on the blood flow is obtained at angiography but is not accessible at ERCP In contrast the ERCP provides information on intrapancreatic inflammatory lesions with emphasis on the abnormalities of the ducts Angiography and ERCP should therefore be considered supplementary methods The use of both methods should improve the diagnostic possibilities and facilitate the selection of cases of pancreatitis amenable to surgery

Acknowledgement

The authors are indebted to Olle Marions for valuable suggestions during the review of the angiograms

SUMMARY

Observations at endoscopic retrograde pancreatography undertaken in 16 cases of chronic pancreatitis have been evaluated by comparing them with the findings at microscopy and surgery and furthermore by correlation to angiography performed in 10 of the cases

ZUSAMMENFASSUNG

Die Beobachtungen die bei der endoskopischen retrograden Pancreatographie (ERCP) bei 16 Patienten mit einer chronischen Pancreatitis erhalten worden waren wurden durch Vergleich mit den Befunden durch die Mikroskopie und Chirurgie und weiterhin durch Korrelation zu den angiographischen Befunden in 10 der Falle ausgewertet

RÉSUME

Les constatations faites au cours de la pancreatographie retrograde endoscopique pratiquée dans 16 cas de pancréatite chronique ont été comparees aux resultats microscopiques et opératoires et en outre aux resultats de l angiographie exécutee dans 10 de ces cas

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RADIOLOGIC APPEARANCE OF FAT IN THE INTERATRIAL SEPTUM OF THE HEART

A SZAMOSI and J RAJS

Recently it was demonstrated that the epicardial fat layer with its extension into furrows and recesses may cause attenuation differences within the normal heart of such a degree that they influence the radiologic image They are spatially related to specific anatomic structures which thus can be outlined and recognized (BERGSTRAND & SZAMOSI 1976 SZAMOSI & JEREB 1977 SZAMOSI 1978 a b)

Occasionally a crescent like narrow zone of diminished attenuation is observed at the center of the heart in the left anterior oblique view at *cineangiography It is* mainly vertically oriented and slightly convex to the right (Fig 1 a) This detail has to our knowledge not previously been mentioned in the literature

In 4 such cases at least one of the atria was outlined by contrast medium during cineangiography performed for other purposes The zone invariably coincided with the interatrial septum the movements of which it also closely followed *(Fig 1 b) In* the case presented the zone could also be discerned on a full size chest film in the appropriate projection (Fig 1 c)

As the locally diminished attenuation suggested the presence of fatty tissue 30 randomly chosen autopsy cases in the material of the Department of Forensic Medicine were examined A well developed fat layer between the muscular walls of the atria as deeply as 1 cm above *the upper limbus* of the oval fossa was found in all cases (Fig 2) The thickness of the fat layer varied between 0 3 and 1 5 cm in adults

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a



b



c

Fig 1 a) Frame of 35 mm cineangiography before injection of contrast medium Left anterior oblique projection Catheter in the right ventricle Zone of diminished attenuation in the middle of the heart Relation to the inferior vena cava b) Cineangiography Small pulmonary vessel phase Beginning of filling of the left atrium The right atrium is still faintly outlined by regurgitant contrast medium Coincidence of zone with the interatrial septum c) Full size chest film with slight lordosis in left anterior oblique view

and between 0 3 and 1 0 cm in 3 children aged 8 to 14 years The fat layer rapidly tapered off as the muscular walls of the atria approached each other

The term interatrial septum is commonly used to denote the structure separating the atria From an embryologic functional and clinical point of view the septum consists of muscular tissue which—due to physical laws and the state of present day



Fig a) Interatrial septum The section is approximately parallel to the atrioventricular plane and 1 cm a bove the upper limbus of the oval fossa The fatty tissue filling out the space between the muscular walls of the atria is evident b) Magnification (3) of the same area from another case

technique—cannot be distinguished on a conventional film from the surrounding heart wall and blood However as WALMSLEY & WATSON (1966) emphasized the interatrial septum contributes only to a minor part of the medial wall of both atria the l ft atrium extends posteriorly and the right atrium anteriorly from this area Thus recesses develop the posterior one is sometimes denoted as the interatrial sulcus From a purely anatomic point of view only the central part of the atrial septum around the oval fossa is formed by the fused muscular wall Between the muscular walls of the left and right atrium a deep cleft exists filled with loose connective tissue and fat (SONDERGAARD et coll 1955) In an early surgical method for closure of atrial septal defects purse string sutures were placed into this cleft in order to approximate the edges of the defect

The radiologic app arance can thus be explained by the fat layer in the interatrial septum which causes the zone of diminished attenuation when tangentially hit by the radiation beam

The practical importance of this phenomenon is limited It may possibly help in determining the correct position of a foreign body e g a catheter within the heart

in relation to the atria It is an intriguing question whether an abnormal thickenss or shape of this fatty layer may indicate lipomatous hypertrophy of the interatrial septum (PRIOR 1964, KINDBLOM & SVENSSON 1977) These rare conditions have been proposed to stand in relation to serious disturbances of the cardiac rhythm and conduction

However, the presented detail contributes to the understanding of the composite nature of the radiologic image of the heart

The fatty tissues present within the pericardial cavity delineate anatomic landmarks to a certain degree, allowing conclusions about the anatomy also without cardioangiography

SUMMARY

The interatrial septum of the heart may be visible on conventional films when it is oriented tangentially to the plane of the incident radiation due to the presence of fatty tissue in the space between the muscular walls of the atria

ZUSAMMENFASSUNG

Das interatriale Septum des Herzens kann auf konventionellen Filmen gesehen werden wenn dieses tangentiell zur Ebene des einfallenden Strahlenganges orientiert ist, infolge des Vorkommens von Fettgewebe zwischen der Muskelwand und dem Atrium

RESUME

Le septum inter auriculaire du cœur peut etre visible sur des radiographies simples quand il est orienté tangentiellement au plan du rayonnement incident grace a la présence de tissus graisseux dans l espace situé entre les parois musculaires des oreillettes

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RADIOLOGIC HEART VOLUME AND SUBSEQUENT MORTALITY

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Radiologic heart volume estimated by the ellipsoid approximation technique from standard chest films (JONSELL 1939) has been accepted into routine clinical practice LINDGREN & ODEN (1954) demonstrated that with careful subject preparation small size miniature films could be used for the purpose and CHRISTIE (1975) that the technique was reliable when the 100 mm films were taken under survey conditions The present report evaluates the power of radiologic heart volume estimated from such films to predict mortality in an unselected male population over the age of 40

Methods

In the Civil Service Health Survey (REID et coll 1974) 12 630 male London civil servants over the age of 40 had both a p a and a lateral 100 mm chest film as part of a cardio-respiratory screening examination A random 10 per cent sample consisting of 1 263 pairs of films was selected and in 1 188 of these radiologic heart volume could be computed The methods and results have been fully reported (CHRISTIE 1975 1978)

A major part of the Civil Service Survey was a follow up of mortality in the screened cohort and 9 years after completion of the survey the deaths in all those subjects who had had a radiologic examination were reviewed (including those cases not in the original sample) The whole set of films was re-evaluated by an independent observer (A G) who was unaware of the current status of each subject It was thus

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Table 1

Deaths at the end of 5 years by quintiles of relative heart volume expected numbers calculated fr m rates for the whole group

Quintile	All cause deaths		Cardiac deaths*		All cardiovascular deaths**	
	Observed	Observed/expected	Observed	Observed/expected	Observed	Observed/expected
1 (low)	26	0.72	10	0.56	10	0.48
2	35	0.88	15	0.75	17	0.77
3	41	0.90	17	0.76	19	0.72
4	45	0.91	26	1.08	30	1.06
5 (high)	86	1.41	46	1.56	58	1.67
n = 1 390	233		114		134	

* ICD (8th Rev) 410–414 420–429

** ICD (8th Rev) 390–409 410–414 420–429 430–458

possible to relate radiologic heart volume to the probability of dying within 5 years of the examination and further to assess the predictive power of the examination with regard to longer term mortality For analysis heart volume was able to be measured in 1 390 subjects 233 of whom had died within 5 years of the examination and 47 more than 5 years afterwards

Radiologic heart volume was calculated for each subject as previously described (CHRISTIE 1975) and corrected for body size after DUBOIS (1927) The resulting corrected heart volume termed relative heart volume was expressed as ml/m² Each subject was then ranked by relative heart volume and the group divided into quintiles each containing 278 subjects All deaths in the cohort were coded after the International Classification of Diseases (ICD) 8th Revision and there is reason to believe that ascertainment was more than 98 per cent complete

Results

The distribution of deaths occurring in the first 5 years by quintile of relative heart volume appears in Table 1 The principal contributor to cardiac deaths (ICD 410-414 420-429) is ischaemic heart disease and the category all cardiovascular deaths (ICD 390–414 420–458) adds mainly deaths from cerebrovascular disease These observed deaths have been related to the numbers expected on the age specific rates for the whole group A highly significant correlation exists between quintile of relative heart volume and proportion of deaths from any cause yet it is apparent that the gradient is produced principally by cardiac and cerebrovascular deaths The distribution of deaths from other causes bears no significant relationship to quintile of heart volume Of all cardiac deaths occurring within 5 years 40 per cent occurred

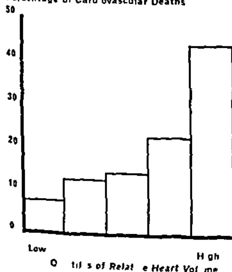
Table 2

Deaths observed more than 5 years after survey by quintile of relative heart volume expected numbers calculated from age specific rates for the whole group

Quintile	No alive after 5 years survey	All cause deaths		Cardiac deaths		All cardiovascular deaths	
		Observed	Observed/ expected	Observed	Observed/ expected	Observed	Observed/ expected
1 (low)	252	6	0 70	4	1 17	4	0 84
2	243	7	0 79	4	1 09	4	0 79
3	237	11	1 12	2	0 47	4	0 68
4	233	11	1 05	4	0 85	8	1 22
5 (high)	192	12	1 31	6	1 50	8	1 40
	1 157	47		20		28	

in the one fifth of the population with the highest relative heart volume as did 43 per cent of total cardiovascular deaths The relative risk carried by men in the highest quintile is 3 04 for cardiac deaths and 3 59 for deaths from any cardiovascular cause The distribution of all cardiovascular deaths by relative heart volume quintile is shown graphically in the Figure

In Table 2 the risk of death occurring more than 5 years after the survey is examined by quintile of original relative heart volume in these men alive at the end of the first 5 year period The numbers of deaths are small yet the number of cardiovascular deaths in the two top quintiles as compared with those in the bottom three



Distribution of cardiovascular deaths within 5 years of survey by quintile of relative heart volume (ml/m²)

is greater than would be expected by chance alone ($p < 0.05$) The power of relative heart volume to predict subsequent mortality extends well beyond the short term

Discussion

The method of computing radiologic heart volume was developed by a group of Swedish radiologists in particular JONSELL, from principles enunciated by ROHRER (1916) HUMERFELDT (1963) used the technique for an epidemiologic survey and LINDGREN & ODÉN showed that the heart volume could be calculated from small size photofluorograms CHRISTIE (1975) calculated heart volume from 100 mm films taken under survey conditions with no subject preparation and showed the results to be reliable

Radiologic heart volume needs to be corrected for body size and if correction for heart rate at the time of examination is possible then the results will be of greater clinical usefulness Heart volume is known to be positively correlated with age and HUMERFELDT TIBBLIN et coll (1967) and CHRISTIE (1978) have shown a strong association with blood pressure The predictive power of relative heart volume (ml/m) for short and medium cardiovascular mortality is unlikely to be independent of blood pressure Nevertheless, under certain circumstances estimation of radiologic heart volume by small size radiography will prove a useful addition to screening tests for cardiovascular disease

SUMMARY

In the London Civil Service Health Survey both p a and lateral 100 mm chest films were taken on 12 630 men aged 40 and above Radiologic heart volume was calculated on a 10 per cent sample and to the sample were added the films of all other subjects from the cohort who had died within 5 years of the survey or more than 5 years afterwards Radiologic heart volume could be calculated on 1 390 subjects of whom 233 had died within 5 years and 47 after 5 years had elapsed For deaths within the first 5 years there was a stepwise increase in mortality with increasing quintile of heart volume Radiologic heart volume predicts death from cardiovascular disease both within 5 years of estimation and for deaths occurring more than 5 years after examination

ZUSAMMENFASSUNG

In der London Civil Service Health Survey wurden sowohl p a als auch laterale 100 mm Brustfilme von 12 630 Männern im Alter von 40 Jahren und daruber gemacht Das rontgenologische Herzvolumen wurde von einer 10 Prozent Gruppe berechnet zu dieser Gruppe wurden die Filme von allen anderen Personen von derjenigen Gruppe die innerhalb von 5 Jahren nach der Untersuchung oder mehr als 5 Jahre danach gestorben waren gefugt Das rontgenologische Herzvolumen konnte von 1 390 Personen festgestellt werden von denen 233 innerhalb von 5 Jahren gestorben waren sowie von 47 nach dieser 5 Jahres Periode Fur die Todesfalle innerhalb der ersten 5 Jahre lag ein schrittweiser Anstieg in der Mortalitat mit ansteigender Quintile des Herzvolumen vor Das rontgenologische Herzvolumen sagt den Tot von einer Cardiovaskularen Erkrankung sowohl innerhalb von 5 Jahren nach der Untersuchung und fur Todesfalle die nach mehr als 5 Jahren nach der Untersuchung auf treten voraus

RESUME

Au London Civil Service Health Survey des ampliphotographies en 100 mm de face et de profil ont éte prises sur 12 630 hommes ages de 40 ans et plus Le volume radiologique du cœur a été calculé sur un échantillon de 10 pour-cent et à cet echantillon ont été ajoutes les films de tous les autres sujets de ce groupe qui etait morts dans les 5 ans suivant cet examen ou apres plus de 5 ans Le volume radiologique du cœur a pu être calcule sur 1 390 sujets dont 233 etaient morts dans les 5 ans et 47 après 5 ans Pour les morts dans les 5 premières annees après l examen il y avait une augmentation de la mortalité proportionnelle a l augmentation du volume cardiaque Le volume cardiaque radiologique permet de prévoir la mort par maladie cardiovasculaire aussi bien dans les 5 ans d estimation que pour les morts survenants plus de 5 ans après l examen

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FROM THE DEPARTMENT OF RADIOLOGY (DIRECTOR PROF P VIRTAMA) UNIVERSITY HOSPITAL SF 20520 TURKU FINLAND

COMPUTER AIDED DIAGNOSIS OF BONE TUMORS

P VIRTAMA K KATEVUO P MÄKELA and E O MAKINEN

The adoption of computer technology in clinical decision making has been relatively slow as compared to the increased use of computers in hospital administration Computer aided diagnostic programs have been used in the analysis of bone tumors (LODWICK et coll 1963) gastric ulcers (WILSON et coll 1965) and heart disease (HALL et coll 1971) demonstrating that Bayes formula of inverse probability is suitable for analysing data derived from radiographic films

Computer aided diagnosis is based on the assumption that systematic analysis of fine radiographic detail results in a more reliable diagnosis than does a more or less subjective impression Computer aided programs can be designed to solve simple differential diagnostic problems by applying statistically significant differences and using the Bayes formula (LUSTED 1968) Such a program may improve the diagnostic result when sufficient expertise with the clinical problem is not available (FRYBACK & THORNBURY 1976) The clinical value of a large computer aided program is still open to question The bone tumor program (LODWICK et coll 1963 LODWICK 1965 LODWICK & REICHERTZ 1968) offers an interesting model for exploration of the effectiveness of such a program in clinical diagnostic decision making

Material and Methods

In computer aided diagnosis descriptive radiologic terms are transferred in digital form and analysed in the computer program the statistical probability is computed for each possible diagnosis

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Table 1

True positive (TP) and false positive (FP) rates (in per cent) of observers A B C and D in different diagnostic groups at 90 and 60 per cent confidence levels

	A		B		C		D		Confidence level
	TP	FP	TP	FP	TP	FP	TP	FP	
Osteosarcoma	88	15	85	18	67	24	70	36	90
(33 cases)	89	24	91	24	76	30	79	48	60
Ewing s sarcoma	87	13	91	17	70	26	74	35	90
(23 cases)	91	17	91	22	74	30	78	43	60
Chondrosarcoma	77	12	81	14	46	23	46	23	90
(26 cases)	85	19	88	15	58	31	50	31	60
Fibrosarcoma	76	19	79	14	62	19	50	24	90
(44 cases)	81	24	86	19	67	24	62	29	60
Benign tumors	69	11	78	18	62	22	69	27	90
(51 cases)	73	13	89	22	67	27	78	31	60
Mean	82	17	86	18	65	28	66	33	

The material comprised *126* malignant and *51* benign solitary bone tumors A short clinical history and pertinent laboratory data were available The radiographic quality of the films varied but films with a low diagnostic information were not included The distribution of malignant tumors appears in Table 1 The *benign* tumors consisted of 4 osteoid osteomas 6 non ossifying fibromas 9 benign cartilaginous tumors 3 *aneurysmal bone cysts* 3 *chondroblastomas* 4 chondromyxoid fibromas 6 cysts 8 benign giant cell tumors and 8 osteochondromas

Four radiologists (*A B C D*) analysed the films A and C were staff members of a university hospital qualified specialists in radiology but with no special expertise in bone radiology D was a third year resident in radiology not yet qualified specialist B in addition to being qualified specialist in radiology had *special experience in* bone radiology and bone tumor diagnosis from working one year at a bone tumor center

Radiologist A used the *computer aided* bone tumor program Two confidence levels of diagnostic decision making were employed one corresponding to 90 per cent of the *computer* response and the other to 60 per cent Diagnoses on a high confidence level (90%) are usually associated with low true positive and low false positive ratios while more liberal criteria of diagnosis lead to a greater percentage of false positive and false negative diagnoses (McNeil et coll 1977)

Results

The percentage of true positive and false positive diagnoses of each observer was calculated for each diagnosis The benign tumors were analysed as one group (Table

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Computer aided diagnosis is based on the assumption that systematic analysis of fine radiographic detail results in a more reliable diagnosis than does a more or less subjective impression. Computer aided programs can be designed to solve simple differential diagnostic problems by applying statistically significant differences and using the Bayes' formula (LUSTED 1968). Such a program may improve the diagnostic result when sufficient expertise with the clinical problem is not available (FRYBACK & THORNBURY 1976). The clinical value of a large computer aided program is still open to question. The bone tumor program (LODWICK et coll 1963, LODWICK 1965, LODWICK & REICHERTZ 1968) offers an interesting model for exploration of the effectiveness of such a program in clinical diagnostic decision making.

Material and Methods

In computer aided diagnosis descriptive radiologic terms are transferred in digital form and analysed in the computer program; the statistical probability is computed for each possible diagnosis.

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improve the result On the other hand the effective size of the data base could be increased by reducing the number of criteria processed by the present model The diagnostic accuracy probably does not change by assuming conditional independence between discriminating criteria to satisfy Bayes theorem although the criteria do exhibit a considerable amount of interdependence

The experience of those who created the present computer aided bone tumor program appears to be filed in a form that is readily understandable and can be used by relatively unexperienced radiologists The use of the program improves diagnostic accuracy significantly and results in improved patient management and cost saving However some work is still needed to improve the present computer program and to develop a generally acceptable clinical strategy in the diagnosis of bone tumors

SUMMARY

Four radiologists three of whom having no special expertise in bone tumor radiology analyzed 177 bone tumors One of the radiologists using a computer aided bone tumor program performed significantly better than the other two at a comparable level of training and was able to compete successfully with the fourth radiologist experienced in bone diagnosis The results validate the assumption that computer aided diagnostic programs may improve the diagnostic accuracy of radiologists having limited experience with the problem at hand

ZUSAMMENFASSUNG

Vier Rontgendiagnostiker von denen drei keine besondere Erfahrung in der Diagnostik von Knochentumoren hatten analysierten 177 Knochentumoren Einer von diesen Rontgendiagnostikern fuhrte unter Verwendung eines Computer unterstutzten Knochentumor programms signifikant bessere Untersuchungen durch als die zwei anderen mit einem vergleichbaren Niveau von Training Seine Resultate waren gleich denen des Rontgendiagnostikers der besondere Erfahrung in der Knochendiagnostik hatte Die Ergebnisse stutzen die Annahme dass Computer unterstutzte diagnostische Programme die Diagnostik des Rontgenologens mit begrenzter Erfahrung verbessern

RESUMÉ

Quatre radiologistes dont trois n avaient pas d expérience speciale dans la radiologie des tumeurs osseuses ont étudie 177 tumeurs osseuses L un des radiologistes utilisant un programme de diagnostic des tumeurs osseuses par ordinateur a eu des resultats significativement meilleurs que les deux autres radiologistes qui avaient un niveau comparable de formation et a été capable de concurrencer avec succès le quatrième radiologiste qui avait une expérience dans le diagnostic osseux Ces résultats confirment l hypothèse que les programmes d aide au diagnostic par ordinateur peuvent améliorer l exactitude du diagnostic de radiologistes ayant une expérience limitée du problème en question

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Table 2

Differences between observers A B C and D in true positive diagnoses of bone tumours at 90 and 60 per cent confidence levels

Observers						Confidence level
A/B	A/C	A/D	B/C	B/D	C/D	
N	S	S	S	HS	N	90
N	HS	HS	HS	HS	N	60

N = no difference S significant difference HS = highly significant difference

1) Inter observer differences in diagnostic accuracy were calculated using the true positive and false positive rates (Table 2)

Discussion

Osteosarcoma and Ewing s sarcoma turned out to be relatively easy diagnostic problems for the computer aided radiologist (A) and the one with experience in bone radiology (B) chondrosarcoma and benign bone tumors appeared to be more difficult for A than for B The diagnostic accuracy in chondrosarcoma was particularly low for C and D and in benign bone tumors for C while D did not succeed well in diagnosing fibrosarcoma In general no significant difference was found between the performance of the computer aided general radiologist (A) and that of the radiologist with experience in bone radiology (B) Nor was there any significant difference between the resident radiologist (D) and general radiologist (C) both of whom performed significantly worse at the 90 per cent level than A or B and still worse at the 60 per cent level

No difference was known to exist between A and C in experience of bone tumor radiology However in this experiment A gained an 82 per cent true positive rate at the 90 per cent confidence level while the corresponding rate of C was only 65 per cent (Table 1) The difference in performance between A and C at both the 90 and 60 per cent confidence levels was highly significant (Table 2) The only reasonable explanation seems to be the computer aided bone tumor program used by A

The level of diagnostic accuracy in the present series is lower than that obtained by LODWICK et coll (1963) This may depend on the material selected for the analysis The present unselected series comprised consecutive cases from different hospitals including several difficult and atypical lesions

The present computer aided program is based on the recognition of numerous fine radiographic details which are not always easily observed on ordinary films An improved quality of the films may raise the diagnostic accuracy The use of special soft tissue radiographic technique additional projections and tomography may also

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FACIAL BONE SCINTIGRAPHY

III Effects of radiation therapy

H F BERGSTEDT and M G LIND

Scintigraphy of the skeleton after administration of bone seeking nuclides for instance technetium diphosphonate ($^{99}Tc^{m}$ DP) is commonly used in the diagnosis of skeletal metastases They are reported to be diagnosed more frequently by scintigraphy than by radiography (SILBERSTEIN et coll 1973 PAPADIMITRIOU et coll 1974 THRALL et coll 1974 BELLIVEAU & SPENCER 1975 OSMOND et coll 1975 BERGSTEDT & HAVERLING 1978) but careful analyses of the true rate of false positive and false negative results are not yet available The close relation between the mucous membranes and the facial bones makes bone involvement by a primary soft tissue tumor likely and neoplastic as well as inflammatory lesions of the facial bones are reported to be detectable by facial bone scintigraphy (BERGSTEDT & LIND 1978)

Neoplastic diseases in the head and neck regions are commonly treated preoperatively by irradiation It is therefore of interest to investigate whether irradiation has any influence on the nuclide uptake in normal and pathologic bone

Material and Methods

Sixteen patients 11 males and 5 females aged 55 to 84 years with carcinoma originating from the mucosa of the oral cavity were given radiation therapy preoperatively Fourteen patients received 40 Gy (4 000 rad) one 64 Gy and one 75 Gy of ^{60}Co irradiation of fields covering the lower anterior part of the face including the

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Table

Regional change of $^{99}Tc^m$ DP uptake in facial bones during radiation therapy in 16 patients with carcinoma of the oral cavity

	Decreased	Unchanged	Increased
Normal bone (n = 16)	0	16	0
Tumor involved bone (n = 7)	1	4	2
Parodontitis (n = 5)	0	5	0
Parodontitis (n = 3)	0	0	3

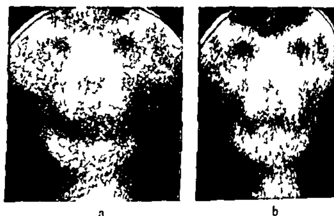
Horizontal bone reduction
Horizontal and vertical bone reduction

caused by parodontitis had before radiation therapy an abnormally high uptake of $^{99}Tc^m$ DP in the alveolar bone affected It was unaltered after irradiation in all but 3 patients The abnormal uptake increased during the course of irradiation in these 3 patients 64 Gy was given to one and 40 Gy to 2 of them They also had vertical reduction of the marginal alveolar bone assumed to indicate the presence of a more active component in the inflammatory reaction of the alveolar bone (Table Fig 2)

Seven patients had a clinically probable tumor invasion of the underlying facial bone and a correspondingly increased uptake of $^{99}Tc^m$ DP In only 3 of these bone involvement was evident at radiography During the period of irradiation the pathologic nuclide uptake increased in 2 but was unaltered in 4 of the 7 patients In one patient a decrease of isotope uptake during the period of treatment paralleled almost complete disappearance of the tumor during this same period as evaluated from repeated clinical examinations (Fig 3) One patient had a buccal carcinoma which initially did not involve the gingiva but during the course of irradiation proceeded to grow and involved the anterior part of the mandible Correspondingly the initially normal distribution of $^{99}Tc^m$ DP was at a second examination following irradiation substituted by a pathologic uptake corresponding to the tumor growth in the mandible which still had a normal radiographic appearance (Fig 4)

Discussion

In general malignant tumors of the facial region are treated by irradiation either pre or postoperatively Knowledge of the extension of tumor growth is decisive in the choice between extensive and more conservative surgery It is therefore important to find out whether or not the underlying facial bones are invaded by tumor growth Facial bone scintigraphy has proved valuable to demonstrate such tumor involvement of the facial bones (BERGSTEDT & LIND) However several different pathologic processes such as chronic sinuitis parodontitis and osteomyelitis may cause an abnormally high uptake of $^{99}Tc^m$ DP in the facial bones (BERGSTEDT & HAVERLING



a b

Fig. 1. Patient without teeth and with sublingual carcinoma. Normal facial bone without tumor involvement. a) Before, b) after irradiation.



a b

Fig. 2. Gingival carcinoma invading the mandible, parodontitis of the superior alveolar bone with horizontal and vertical bone reduction. a) Before, b) after irradiation.

tumor region and the regional lymph nodes. The irradiation was fractionated into daily doses of 2 Gy, 5 days a week.

Each patient was examined with a gamma camera before and about one week after the radiation therapy period (Nuclear Chicago Pho Gamma IV). The examination was performed 5 hours after the intravenous injection of 370 MBq (10 mCi) $^{99}Tc^{m}$ DP. A.p., right and left lateral projections were obtained. 300 000 counts were collected in each projection. Conventional radiography and orthopantomography were performed in all patients.

Eight patients had no teeth and 8 had teeth to a varying amount. All of these patients had a horizontal reduction of the marginal alveolar bone equivalent to one third to one half of the root length and 3 also local vertical alveolar bone reduction as assessed by orthopantomography.

Results

The clinically and radiologically normal facial bones in all 16 patients had a normal and a symmetric distribution of $^{99}Tc^{m}$ DP both before and after radiation therapy. The irradiation did not cause any demonstrable change of the uptake in the normal bone (Table, Fig. 1).

All 8 patients with teeth and marginal horizontal reduction of the alveolar bone



a b

Fig 4 Patient without teeth and with buccal carcinoma initially not involving the gingiva but growing during the course of treatment and invading the mandible after irradiation a) Before b) after irradiation

It may be concluded that facial bone scintigraphy for defining possible tumor involvement of the facial skeleton should be performed before radiation therapy which if successful may revert a pathologic uptake to normal Furthermore the scintigraphic abnormality caused by parodontitis may increase during treatment If this source of error is kept in mind repeat scintigraphy may be used to establish whether bone involvement has occurred or increased during the irradiation

SUMMARY

The uptake of • Tc^m DP in normal facial bones was not changed by irradiation of malignant tumors The intensity of the pathologic uptake into regions with active parodontitis in a few patients increased during irradiation The uptake of $^{99}Tc^m$ DP in bone with neoplastic growth varied during the period of treatment probably depending on the tumor reaction to irradiation

ZUSAMMENFASSUNG

Die Aufnahme von $^{99}Tc^m$ DP in bestrahlten normalen Gesichtsknochen wurde nicht durch Bestrahlung von malignen Tumoren geändert Die pathologische Aufnahme in Regionen mit aktiver Paradentitis bei einigen Patienten stieg während der Bestrahlung Die Aufnahme von $^{99}Tc^m$ DP im Knochen mit neoplastischen Wachstum variierte während der Behandlungsperiode wahrscheinlich in Abhängigkeit von der Tumorreaktion auf die Bestrahlung

RÉSUMÉ

La fixation de $^{99}Tc^m$ DP sur les os de la face normaux irradiés n a pas été modifiée par l irradiation de tumeurs malignes L intensité de la fixation pathologique sur les régions atteintes par une parodontite active a augmenté chez quelques malades au cours de l irradiation La fixation de ^{99}Tc DP dans l os atteint de tumeur maligne a varié au cours de la période de traitement probablement sous l influence de la réaction de la tumeur à l irradiation

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Fig 3 Gingival carcinoma engaging the mandible clinically almost disappearing during the course of irradiation a) Before b) after irradiation

BERGSTEDT & LIND) i e the results of facial bone scintigraphy may then be falsely considered as indication of malignant involvement of the bone tissue

Irradiation is known to cause morphologic changes of the bone structure Thus hypothetically radiation therapy might influence the capacity of the bone substance to take up intravenously injected $^{99}Tc^{m}$ DP (RÉGAUD 1922 WATSON & SCARBOROUGH 1938 WILDERMUTH & CANTRIL 1953, RUBIN & CASARETT 1968, COX 1974 LIND & NATHANSON 1977 NATHANSON & BACKSTRÖM 1978) LIND & NATHANSON have demonstrated that irradiation of rabbit skull bones with a dose high enough to cause histologic changes of the bone structure did not cause a demonstrable change of the $^{99}Tc^{m}$ DP uptake However at irradiation of normal bone with local inflammatory or neoplastic lesions the situation is more complex

The results of the present series demonstrate that the uptake of $^{99}Tc^{m}$ DP in normal facial bone was not affected by irradiation which was in accordance with the results of the animal experiments (LIND & NATHANSON) However the abnormally high uptake caused by an active inflammatory parodontic process with both horizontal and vertical reduction of the alveolar bone increased in 3 patients during irradiation This parallels the clinical experience that an aggravation of the parodontitis is to be expected during radiation therapy including the alveolar regions

Such reactions obviously constitute a source of error and as a control measure the dental and alveolar condition of the patient should always be assessed clinically and radiographically before the evaluation of facial bone scintigrams especially if these are obtained after radiation therapy (BERGSTEDT & LIND)

Neoplastic involvement of bone causes an increased uptake of $^{99}Tc^{m}$ DP This effect is probably dependent on the tumor growth rate and an increased metabolic activity in the adjacent bone tissue Some tumors were unaffected by irradiation or even increased during the course of treatment (Fig 4) Two patients with such tumors had increasingly pathologic uptake of nuclide during the period of the treatment Another patient had a decreased pathologic accumulation concurrent with a disappearance of the tumor However the correlation between scintigraphic assessment and progression or regression of neoplastic growth in bone tissue is not known in detail and at the present time it is not possible to foresee the clinical course of a tumor from a change of pathologic uptake at bone scintigraphy

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ARTHROGRAPHY IN DISLOCATION OF THE ACROMIOCLAVICULAR JOINT

BENGT E ZACHRISSON and ARVID EJESKAR

The lateral end of the clavicle is attached to the acromion by the capsule of the acromioclavicular joint strengthened with the acromioclavicular ligament and to the coracoid process by the coracoclavicular ligament The latter is divided into two parts a lateral part the trapezoid ligament and a medial part the conoid ligament The conoid ligament is attached to the dorsal medial part of the coracoid process while the attachment of the trapezoid ligament lies ventrally and slightly lateral to the conoid ligament Lateral to these ligaments is the coraco acromial ligament which binds the anterior part of the acromion to the lateral dorsal part of the coracoid process (Fig 1)

When dislocation of the acromioclavicular joint occurs it is believed that the acromioclavicular ligament is ruptured as well as the trapezoid and conoid parts of the coracoclavicular ligament (ALLMAN 1967 DEBEVOISE & BROWN 1968 WEAVER & DUNN 1972) However it has been shown experimentally that the acromioclavicular joint may also become dislocated when the acromioclavicular ligaments are intact (URIST 1946 EJESKAR unpublished data)

Dislocation of the acromioclavicular joint is usually diagnosed at the clinical examination or by radiography with or without weight application on the acromio clavicular joint and hence it is not possible to gain exact information on the extent of the injury to the ligaments In 1962 FISCHETTI stated that arthrography could be used for this purpose but to judge from the literature this method does not seem to have been used by others As one of the measures used in the preoperative examina

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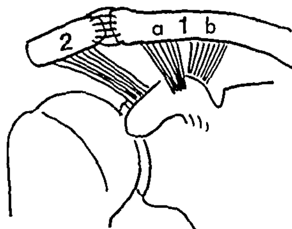


Fig 1 Schematic drawing of the ligaments around the acromioclavicular joint 1 Coracoclavicular ligament divided into (a) trapezoid ligament and (b) conoid ligament 2 Coraco acromial ligament The figures are placed above the respective ligaments

tion of patients with dislocation of the acromioclavicular joint arthrography has been tried at this hospital to ascertain whether it can give information regarding the severity of the ligament injury

Method and Material

Arthrography With the patient in the supine position the acromioclavicular joint was palpated and marked out After local anesthesia in the skin the joint was punctured with a fine needle (OD 0 9 mm) directed dorsally and caudally The joint was usually reached after the needle had been passed in for a distance of about 1 to 1 5 cm under the skin The position of the needle in the joint was confirmed by aspiration of joint fluid and by TV monitoring or films When the joint was punctured bloody joint fluid was often aspirated When the needle was suitably positioned the *contrast medium about 5 ml Urografin 45 % was injected at first* without much resistance Towards the end of the injection the patient experienced a slight feeling of pressure in the region of the acromioclavicular joint and at the same time increased resistance was noted during the injection After the termination of the injection the shoulder region was mobilized and if possible the patient was turned round once on the examination couch in order to spread the contrast medium within the area of the rupture A p views of the acromioclavicular joint were obtained with the patient supine and with beam directions of 0 15 and 30° cranially and 15° and 30 caudally Lateral views of the shoulder joint region were then exposed with the patient in the standing or the sitting position

Arthrography of the acromioclavicular joint was performed in 10 patients One patient was excluded from the material because the films could not be assessed due to incorrect injection of the contrast medium The other 9 patients one woman and 8 men ranged in age from 23 to 51 years In all these cases the clinical diagnosis was dislocation of the acromioclavicular joint on the right side in 5 and on the left side in 4 instances The arthrography was carried out 1 to 8 days after the injury Seven

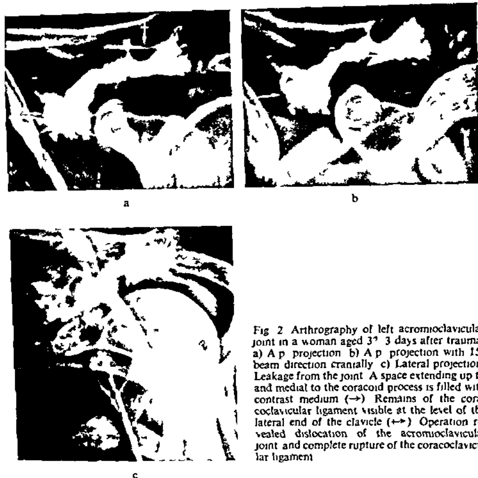


Fig 2 Arthrography of left acromioclavicular joint in a woman aged 37 3 days after trauma a) A p projection b) A p projection with 15 beam direction cranially c) Lateral projection Leakage from the joint A space extending up to and medial to the coracoid process is filled with contrast medium (→) Remains of the coracoclavicular ligament visible at the level of the lateral end of the clavicle (↔) Operation revealed dislocation of the acromioclavicular joint and complete rupture of the coracoclavicular ligament

patients were operated upon 1 to 2 days after arthrography and one patient underwent operation six months after injury One patient was treated conservatively

Operation In recent dislocations of the acromioclavicular joint the joint was exposed and the coracoclavicular ligaments identified The dislocation was reduced and the clavicle fastened to the coracoid process by wiring (EJESKAR 1974) In one patient a lateral clavicular resection was performed six months after the injury

Results

Operation In the 7 patients operated upon at an early stage the dislocation of the acromioclavicular joint was confirmed In addition it was found that the lateral end of the clavicle had become loosened from the surrounding ligaments and muscles Complete rupture of the coracoclavicular ligament was observed in 4 cases and in 3

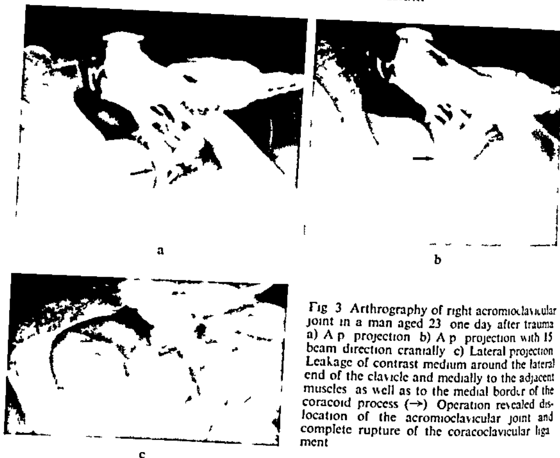


Fig 3 Arthrography of right acromioclavicular joint in a man aged 23 one day after trauma a) A p projection b) A p projection with 15 beam direction cranially c) Lateral projection Leakage of contrast medium around the lateral end of the clavicle and medially to the adjacent muscles as well as to the medial border of the coracoid process (→) Operation revealed dislocation of the acromioclavicular joint and complete rupture of the coracoclavicular ligament

instances the rupture was subtotal (incomplete) involving the whole of the trapezoid ligament and the greater part of the conoid ligament This was also the case in the patient operated upon six months after the injury

Arthrography The best information was obtained with a p projections with beam directions of 0 15 and 30 cranially

Leakage of contrast medium around the lateral end of the clavicle In 8 patients the contrast medium had leaked around parts of the lateral end of the clavicle indicating that this end had become detached from surrounding muscles and ligaments (Figs 3 4) Contrast leakage longitudinally in the muscles was also observed in 5 of these cases (Figs 3 5)

Leakage of contrast medium towards the coracoid process In all cases leakage of the medium medially ventrally and caudally with a fairly well delimited partly slit shaped space filled with contrast medium and extending from the acromioclavicular joint towards the coracoid process was consistently observed Anatomically the lateral caudal border of this cavity consisted partly of the coracoacromial ligament In 4 cases the slit extended to the medial border of the coracoid process



Fig. 4 Arthrography of left acromioclavicular joint in a man aged 33 5 days after trauma a) A p projection b) Lateral projection The lateral end of the clavicle is surrounded by contrast medium and medium has *leaked from the joint and flowed in the direction of the coracoid process* but has not reached the medial border of the coracoid Operation revealed dislocation of the acromioclavicular joint The medial part of the conoid ligament was intact but the rest of the coracoclavicular ligament was ruptured



Fig 5 Arthrography of right acromioclavicular joint in a man aged 41 2 days after trauma. a) A p projection b) A p projection with 15 beam direction cranially Leakage of contrast medium from the joint to the muscles medially and towards the middle portion of the coracoid process (→) The medial border of the space does not reach the medial part of the coracoid process At resection of the lateral *part of the clavicle six months later intact remains of the conoid ligament* were found but the rest of the coracoclavicular ligament was ruptured

and to a point slightly medial to it (Figs 2 3) while in 5 cases the contrast medium did not pass the medial part of the coracoid (Figs 4 5) In a few cases contrast defects were observed at the lateral end of the clavicle at the site of the coracoclavicular ligaments (Fig 2)

Comparison between operative and arthrographic findings Leakage of contrast medium beyond the medial part of the coracoid process corresponded to complete

rupture of the ligaments at operation (4 cases) and leakage not going beyond that limit to a subtotal ligament rupture (4 cases) The conservatively treated patient belonged to the latter group with respect to the arthrography, and a diagnosis of incomplete rupture of the ligaments was therefore considered adequate

Discussion

Opinions differ among clinicians, as to whether dislocation of the acromioclavicular joint should be treated conservatively or operatively The varying results obtained with the different methods of treatment may perhaps be explained by heterogeneity of the material with respect to the severity of the ligament injury It has been difficult, without operative intervention to diagnose the extent of the injury to the ligaments

In arthrography of the acromioclavicular joint only the narrow joint space is filled normally (WESTON 1974) On the other hand when the joint is dislocated leakage of contrast medium occurs In the light of the concordant operative and arthrographic findings in ligament injuries of the same type it is considered that the distribution of the leaking contrast medium in relation to the coracoid process will give information regarding the severity of the injury to the ligaments In all the patients with complete rupture of the coracoclavicular ligament for instance leakage from the acromioclavicular joint to the site of the insertion of this ligament on the coracoid process and even medial to this area was observed, whereas in those with subtotal (incomplete) rupture the leaking medium did not spread so far in the medial direction The examination is easy to perform and in the supine position no cooperation on the part of the patient is necessary Periarticular injection of the contrast medium is a source of error that should be borne in mind since this prevents an adequate assessment of the ruptured area Thus it should be possible to demonstrate with the aid of arthrography rupture of the ligaments also in cases in which clinical and radiologic stability testing has for various reasons proved difficult

SUMMARY

Arthrography was performed in 10 patients with dislocation of the acromioclavicular joint The examination was unsuccessful in one case In the remaining 9 patients leakage of the contrast medium was observed around the joint and in the direction of the coracoid process The arthrographic abnormalities were compared with the findings at operation The distribution of the medium that had leaked out provided information on the severity of the injury to the ligaments

ZUSAMMENFASSUNG

Eine Arthrographie wurde bei 10 Patienten mit Dislokation des Acromioclavicular Gelenks vorgenommen Die Untersuchung war nicht erfolgreich in einem Fall Bei den übrigen 9 Patienten wurde ein Austritt des Kontrastmittels um das Gelenk herum und in

-Richtung auf den Processus coracoideus beobachtet Die arthrographischen Veranderungen wurden mit den Befunden bei der Operation verglichen Die Verteilung des Kontrastmittels um das Gelenk herum vermittelte eine Information uber den Grad der Schadigung des Ligaments

RÉSUME

Une arthrographie a été faite chez 10 malades atteints de luxation de l articulation acromioclaviculaire L examen a échoué dans un cas Chez les 9 autres patients on a observe une fuite du moyen de contraste autour de l articulation et dans la direction de l apophyse coracoide Les anomalies arthrographiques ont éte comparees aux constations opératoires La distribution du moyen de contraste qui avait fui hors de l articulation a fourni des renseignements sur la gravite des lesions ligamentaires

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ARTHROSIS OF THE ANKLE EVALUATED ON FILMS IN WEIGHT-BEARING POSITION

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The value of films exposed in weight bearing positions in the evaluation of arthrosis of the knee has been emphasized by AHLBACK (1968) No corresponding investigation of the ankle joint has been found in the literature At follow up examinations of patients treated for malleolar fractures such films were included

Material and Methods

Repeat examination of 113 patients 69 women and 44 men (mean age 43 6 years women 43 6 men 43 5 range 16–77 years) was performed about 7 years after the date of fracture (mean 83 9 months range 68–98 months) The fractures were classified as follows Type A—Transverse fibular fracture distal to the syndesmosis Type B—Oblique fibular fracture at the level of the syndesmosis with or without rupture of the tibiofibular ligament Type C—Oblique fibular fracture proximal to the syndesmosis with rupture of the tibiofibular ligament (Fig 1)

Both ankles were examined in all patients with a standardized technique The patient supine vertical beam direction and three views—straight a p (lateral margin of the foot 90 to the horizontal plane a p with the limb medially rotated 20 and a lateral view with the leg and foot laterally rotated 85 If necessary further films were exposed to obtain the best possible demonstration of the joint surfaces Reproducible angles were obtained by using the device described by BOLIN (1961)

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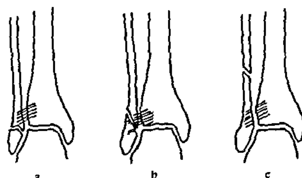


Fig 1 Classification of fractures a) Transverse fibular fracture distal to the syndesmosis (type A) b) Oblique fibular fracture at the level of the syndesmosis with or without rupture of the tibiofibular ligament (type B) c) Oblique fibular fracture proximal to the syndesmosis with rupture of the tibiofibular ligament (type C)

Table 1

Classification of arthrosis according to MAGNUSSON *and* CEDELL

)egree	Roentgenologic abnormality of the joint
)	Slight reduction of joint space and slight formation of osteophytes on joint margins
+	More marked abnormalities possibly with addition of a sclerotic zone within subchondral osseous tissue of tibia
+	Joint space only about half as high as on uninjured side and rather marked formation of osteophytes
+ + +	Joint space has completely or almost disappeared

Table 2

Radiologic grading of arthrosis in 113 cases at the time of follow up in relation to the initial type of fracture

Degree	Type of fracture		
	A	B	C
0	2	30	1
(+)	3	41	5
+	1	12	0
+ +	0	12	2
+ +	0	4	0

In 110 of the 113 patients films in weight bearing position could be obtained The body weight was equally divided on both feet One film was exposed with horizontal a p beam direction with the limb rotated 20 medially When necessary to obtain a clear view of the joint space between the talus and the lateral malleolus further films in slightly altered projections were exposed The same technique was applied

a b

Fig 2 a) Patient supine b) View at weight bearing Arthrosis classified as + at both examinations.

a b

Fig 3 a) Patient supine Arthrosis classified as + b) View at weight bearing Arthrosis classified as + +

in 24 patients initially treated at this hospital but now living elsewhere and examined by the authors at radiology departments in the residential areas of the patients. The arthrosis was classified according to MAGNUSSON (1944) and CEDELL (1967) (Table 1)

Results

The degree of arthrosis in the different types of fracture at the time of follow up is listed in Table 2. In only 2 of 220 ankle joints examined did films exposed in standing add to the information provided by the films with the patients in supine position. In both cases a slight reduction of the distance between the talus and the tibial surface could be measured at weight bearing. In one case the same degree of arthrosis was present at both types of examination, in the other case + was re-classified to + + on weight bearing (Figs 2, 3)

Discussion

In slight arthrosis of the ankle joint a local narrowing of the joint space may be present, most often in the lateral aspect. In view of the arched form of the joint in the sagittal plane any narrowing present in the anterior or posterior parts of the joint cannot be demonstrated by a p beam direction. This may explain why only two cases with more marked narrowing of the joint space were found at weight bearing since no lateral films were exposed of the joints in standing position. Thus additional projections, when necessary, achieved by fluoroscopy and tomography would most probably have added to the information. However, this would be too time-consuming for routine use and was therefore refrained from. Also, in cases of advanced arthrosis films in weight bearing position did not demonstrate the abnormality of the joint space any better than did the conventional examination.

Conclusion. Contrary to what AHLBACK has stated to apply for the knee, films of the ankle joint in weight bearing position do not give further information in relation to the amount of extra work and increased radiation dose.

SUMMARY

About 7 years after a malleolar fracture 113 patients were examined for development of arthrosis. The addition of films exposed in weight bearing position with a p beam direction to views of the ankle joint exposed in supine position did not contribute to the diagnosis of arthrosis.

ZUSAMMENFASSUNG

Etwa 7 Jahre nach einer Knöchelfraktur wurden 113 Patienten hinsichtlich der Entwicklung einer Arthrose untersucht. Zusätzliche Filme in Belastungsposition mit einer a p Strahlenrichtung, um das in aufrechter Stellung exponierte Fussgelenk darzustellen, trug nicht zur Diagnose einer Arthrose bei.

RESUME

Cent treize patients ont été examinés environ 7 ans après une fracture malleolaire externe pour rechercher l apparition d une arthrose La comparaison de films pris en charge avec une direction antéro postérieure du rayonnement et de radiographies de la cheville prises en decubitus ne contribue pas au diagnostic d arthrose

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CLINICAL SIGNIFICANCE OF DUODENAL DIVERTICULA AND VALUE OF HYPOTONIC DUODENOGRAPHY

P J LUKES P ROLNY A E NILSON and R GAMKLOU

Duodenal diverticula were first described by CHOMEL (1710) and demonstrated roentgenologically in 1912 by CASE (1916) The clinical significance of duodenal diverticula is a matter of controversy (LIEBERMAN & RAMOS 1963 LANDOR & FULKERSON 1966 JULER et coll 1969) Diverticula have sometimes been considered of importance in the pathogenesis of liver biliary and pancreatic disease (CHITAMBER & SPRINGS 1953 SVARTZ & SJOBERG 1953 ROLNY et coll 1976 OSNES et coll 1977) Occasionally acute complications such as diverticulitis with perforation compression of the common bile duct with jaundice and pancreatitis or gastrointestinal hemorrhage may occur (NEIL & THOMPSON 1965 MUNNEL & PRESTON 1966 SOLHAUG & SEMB 1974)

The radiographic diagnosis of duodenal diverticula has been based on routine barium examinations of the stomach and the duodenum During the past decade an anomalous insertion of the common bile duct into a diverticulum has been recognized as sometimes complicating biliary tract disease This anomaly has been diagnosed at operative or postoperative cholangiography often combined with an upper gastrointestinal tract barium examination (CULVER & PIRSON 1966) In 1967 COSTOPOULOS & MILLER employed simultaneous transhepatic cholangiography and hypotonic duodenography for preoperative diagnosis of possible anomalous insertion of the common bile duct into a diverticulum in patients with obstructive jaundice EATON et coll (1969) reported on a patient with jaundice in whom preoperative

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Fig 1 Postoperative cholangiography Narrowing and irregularity of the terminal portion of the common bile duct—stenosing papillitis

diagnosis of juxtapapillary diverticula was made at hypotonic duodenography only. They pointed out that this anatomic condition may disturb the ampullary sphincter mechanism and interfere with the emptying of the common bile duct

In recent years more and more attention has been drawn to the duodenal diverticula because of improved diagnostic means and because of increasing cognizance of the possibility of the lesion being of clinical significance Thus OSNES et coll reported on the value of endoscopic retrograde cholangiopancreaticography (ERCP) in the diagnosis of juxtapapillary diverticula

The present report describes clinical findings in patients with duodenal diverticula and the experience at this hospital with hypotonic duodenography in the diagnosis of diverticula

Material and Methods

The material consisted of 24 patients 13 men and 11 women aged between 38 and 88 years (mean age 63 years) with duodenal diverticula The diverticula were found at hypotonic duodenography of 90 consecutive patients all with upper gastrointestinal symptoms of long standing mostly suggesting a pancreatic or biliary origin

The hypotonic duodenography was performed according to the double contrast technique described by BILBAO et coll (1968) with the following modification Hypotonia was induced by an intravenous instead of an intramuscular injection of 60 mg propantheline bromide (Pro Banthine) Mucosal anesthetics in the duodenum

:re not used In one patient hypotonic duodenography was carried out simul neously with a postoperative cholangiography The position size and number of ie diverticula were recorded No complications occurred

All patients had undergone basic clinical and laboratory examinations of the pper gastrointestinal tract In 19 patients a conventional barium examination of ie stomach and duodenum had previously been performed and in 4 cases duodenal iverticula had been observed All these films were reexamined and compared ith the results obtained at hypotonic duodenography The exocrine pancreas inction was examined by a secretin CCK test in 18 patients During the test samples f duodenal juice were obtained from the duodenal loop for bacteriologic ulture in 11 patients The results were compared with the findings in a control roup of 26 patients of comparable sex and age distribution but without diverticula Vine of the controls had chronic pancreatitis The remaining 17 control patients iad no evidence of liver biliary or pancreatic disease Two of the 9 patients had reviou ly been operated upon In one patient a pancreaticojejunostomy with a Roux-en Y anastomosis had been performed and in the other a duodenojejunostomy because of a superior mesenteric artery syndrome

Results

In 18 of the 24 patients (75) diverticula were located in the second portion of the duodenum within 2 cm of the papilla of Vater In one of these cases the common bile duct entered the papilla immediately distal to the neck of the diverticulum Disturbance of the emptying mechanism of the common bile duct and indication of st nosing papillitis were demonstrated by simultaneous postoperative cholangiography and hypotonic duodenography (Figs 1 2 3) In this case concrements in the common bile duct were also found at laparotomy Three patients had two diverticula In 5 patients the diverticula were located in the third part of the duodenum and in one in the fourth part Conventional barium examination of the stomach and duo d -m wa performed in 19 patients and duodenal diverticula were found in 8 In 18 th pancreatic function was analysed and was found to be reduced in 9

B cteriologic culture of the duodenal aspirate was p rformed in 11 patients and w s positive in 9 (more than 100 000 microorganisms/ml) Two of these had achylia after pentagastrin stimulation All 26 patients in the control group had normal gastric acid ecretion and a ignificant quantity of microorganisms was found in the duodenal juice of only the 2 patients with a chronic pancreatitis and previously operated upon The remaining 24 pati nts had n gative bacteriologic cultures

Based on clinical or laboratory data operative or autopsy findings the final diagnosis for the 24 patients with diverticula was liver disease with or without biliary tract disease in 6 pancreatic disease in 11 (including 2 carcinomas) and in 7 p tients miscellaneous conditions but without hepatic pancreatic or biliary disease





Fig. 2 Fig. 3

Fig. 2. Relationship between diverticula, common bile duct and pancreatic ducts demonstrated at simultaneous hypotonic duodenography and postoperative cholangiography.

Fig. 3. Marked compression and dilatation of the common bile duct due to pressure of diverticula causing delayed emptying.

Discussion

The frequency of duodenal diverticula demonstrated at gastrointestinal radiography varies from 0.016 to 5.6 per cent and at autopsy from 5 to 22 per cent (RANKIN & MARTIN 1934, ACKERMANN 1943, CHITAMBER & SPRINGS). About 62 per cent of the diverticula occur in the second portion of the duodenum within 2.5 cm from the papilla of Vater, 30 per cent in the third and 8 per cent in the fourth part of the duodenum (NEIL & THOMPSON). In the present series of 90 patients examined by hypotonic duodenography duodenal diverticula were found in 27 per cent. However, the high percentage may be explained by the fact that this is a material selected from patients with upper gastrointestinal symptoms mostly suggesting a pancreatic or biliary origin. The distribution of the diverticula between different parts of the duodenum was similar to what has previously been reported.

A routine radiography of the upper gastrointestinal tract might reveal a duodenal diverticulum. The incidence of detected diverticula is however smaller at routine examinations than at examinations where special attention is paid to this condition (CHITAMBER & SPRINGS). Inflammatory narrowing of the neck of the diverticula or

filling of the diverticular cavity by duodenal contents may keep the barium from entering the diverticulum which thus is not demonstrated The fact that a small diverticulum may be masked by contrast medium in other parts of the small bowel is another reason for missing the diagnosis Therefore in patients with symptoms which could be related to duodenal diverticula repeated examinations have been recommended (SOLHAUG & SEMB)

With routine barium examinations 4 of 8 diverticula were primarily not reported but were found on reexamination of the films Thus in the present series only 8 of 19 routine barium examinations revealed diverticula

The coexistence of duodenal diverticula and diseases of liver biliary tract and pancreas is remarkable The present findings of significant quantities of micro-organisms in the duodenum despite normal gastric acid secretion are in contrast to previous reports (TABAQCHALI 1970) They may be a factor of importance in the pathogenesis of associated diseases in patients with duodenal diverticula In the present series significant differences existed between the results of the bacteriologic culture in the patients with diverticula and in the controls The only 2 patients in the control group in whom the culture was positive had previously been operated upon In both cases serious changes in the duodenal motility and emptying might be the reason for the presence of the bacterial flora in the duodenum

Besides the juxtapapillary localization the size of the diverticula may play an important role in the pathogenesis of associated diseases due to influence on duodenal pressure motility and emptying The consequences might be stagnation of duodenal contents which may become a suitable substrate favouring the growth of microorganisms

Hypotonic duodenography is a safe and easily performed examination It requires no special equipment or skill and it seems to reveal with high accuracy the exact localization size and number of diverticula Since duodenal diverticula may predispose to liver biliary and pancreatic diseases a meticulous examination of the duodenum is recommended in every patient with symptoms from the upper gastrointestinal tract

When duodenal diverticula are revealed further examinations should be focused on the liver the biliary tract and the pancreas Special attention should be paid to those patients in whom juxtapapillary diverticula are found or when the papilla of Vater is located in a diverticulum As pointed out by several authors and as documented in one of the present patients this anatomic anomaly interferes with the emptying of the biliary and pancreatic duct systems predisposing to stasis and other complications

Conclusions The clinical significance of duodenal diverticula in the pathogenesis of liver biliary and pancreatic disease is suggested Diverticula are easily diagnosed by hypotonic duodenography When duodenal diverticula are found and associated with upper gastrointestinal symptomatology further examinations of the liver biliary



Fig 2



Fig 3

Fig 2 Relationship between diverticula common bile duct and pancreatic ducts demonstrated at simultaneous hypotonic duodenography and postoperative cholangiography

Fig 3 Marked compression and dilatation of the common bile duct due to pressure of diverticula causing delayed emptying

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tract and pancreas should be performed Special attention should be paid to patients with juxtapapillary diverticula

SUMMARY

In 24 patients duodenal diverticula were found by means of hypotonic duodenography Nineteen of these patients had also undergone a conventional barium examination but with that procedure the diverticula were revealed in only 8 of them The clinical significance of duodenal diverticula is suggested and the diagnostic value of hypotonic duodenography is emphasized

ZUSAMMENFASSUNG

Ein Duodenaldivertikel wurde bei 24 Patienten unter Verwendung der hypotonischen Duodenographie gefunden Neunzehn dieser Patienten waren auch einer konventionellen Barium Untersuchung unterzogen worden mit diesem Verfahren wurden jedoch nur in 8 ein Divertikel festgestellt Auf die klinische Bedeutung des Duodenaldivertikels wird hingewiesen und der diagnostische Wert der hypotonen Duodenographie hervorgehoben

RÉSUMÉ

Des diverticules duodenaux ont été trouvés chez 24 malades grace a la duodénographie hypotonique Dix neuf de ces malades avaient aussi subi un examen baryté classique mais par cette technique les diverticules n ont été mis en évidence que dans 8 cas Les auteurs envisagent l importance clinique des diverticules duodénaux et soulignent l intéret diagnostique de la duodénographie hypotonique

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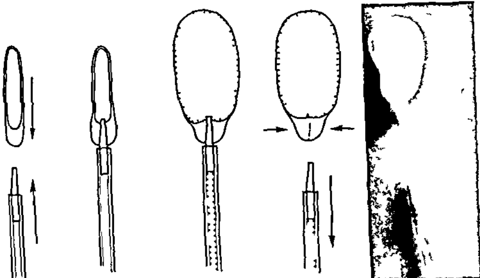


Fig 1 The elongated solid neck of the latex rubber balloon is penetrated by the steel tube and the balloon can be inflated with liquid When the catheter with the steel tube is withdrawn the neck of the balloon closes tightly and the balloon remains inflated

by percutaneous puncture or by puncture after surgical exposure After an initial angiography outlining the cervical and cranial arteries the thin catheter was re placed by either a Seldinger needle or a large bore catheter through which the balloon catheter was introduced The balloon was placed selectively in either the internal or external carotid artery or into one of their branches The balloon was then inflated with Isopaque Cerebral and detached from the tip of the catheter Finally a second angiography was performed the catheter removed and the artery sutured In 2 pigs a third angiography was carried out 4 weeks later

The balloon catheter constructed by LAITINEN (marketed by Emset Oy Helsinki Finland) consists of an inflatable balloon made of natural latex rubber attached to the tip of a polyethylene catheter (ID/OD 0 4/0 63 mm) by means of a thin stainless steel tube 2 5 mm long (Fig 1) The distal half of the steel tube is tapered to an outer diameter of 0 2 mm in order to make possible its penetration into the elongated solid neck of the balloon The size of the deflated balloon is 0 6 mm × 4 0 mm and it is inflatable to 5 0 mm 9 0 mm when filled with a volume of approximately 0 1 ml Positioned in a vessel the balloon gradually becomes fixed in place when in flated and may then be detached simply by withdrawal of the catheter

Results

In total 6 balloons were successfully inflated and detached in various vessels In each case the position of the balloon was confirmed by angiography (Fig 2) One pig died before the balloon had been detached from the catheter and 2 pigs died

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OCCLUSION OF THE CAROTID ARTERY USING CATHETER WITH DETACHABLE BALLOON IN PIGS

B LILIEQUIST L LAITINEN Å FORSSELL and S WIRELL

Balloon catheters for intravascular occlusion of arteries and veins were introduced in general surgery by FOGARTY et coll (1963) In neurosurgery a similar technique was reported by LUESSENHOP & SPENCE (1964) and the intracranial use of an arterial flow directed balloon catheter was later in detail explored by SERBINENKO (1971 1974 a) This author also reported upon the use of a detachable balloon for intra vascular occlusion of arteriovenous fistulae and saccular aneurysms (SERBINENKO 1974 b) His technique has since been revised by DEBRUN et coll (1975 a) PROLO et coll (1977) GUILLAUME & ROULLEAU (1977) PEVSNER (1977) and WHOLEY (1977) each using their own slightly modified catheters The basic requirements necessary for an optimally designed flow directed detachable balloon catheter were settled by PEVSNER Recently LAITINEN & SERVO (1978) described a new detachable and self sealing balloon Only few reports on experimental occlusion of vessels with a detach able balloon have appeared (DEBRUN et coll 1975 b GUILLAUME & ROULLEAU PEVSNER) The present report concerns the first results of carotid artery occlusion in pigs using the balloon catheter designed by LAITINEN & SERVO

Material and Methods

Five pigs weighing between 30 and 50 kg were used for the experiments The catheterization procedure was performed under general anesthesia A catheter (Cook ID/OD 1 50/2 26 mm) was introduced into the common carotid artery either

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Several balloons collapsed and embolized peripherally after being detached from the catheter In some cases the balloons leaked after having been introduced into the vessel However most of the balloons could be inflated and deflated repeatedly with no evident leakage and the balloon catheter could even be removed and then reinserted into the vessel By using the guide catheter the balloon could be selectively placed in any of the major branches of the external carotid artery

Discussion

The intention of the present experiments was to work out a method for occlusion of cerebral arteries in pigs that could also be used in man Catheterization of the common carotid artery was first attempted using the Seldinger technique simulating as closely as possible the conditions in man However it was soon evident that the introduction of a balloon catheter with this technique was not practically possible in pigs and a surgical approach was employed

Guiding and directing the ballooned tip of the catheter was not difficult the catheter could easily be introduced into the internal as well as into the external carotid artery and their major branches No difficulties were encountered in releasing the inflated balloon from the tip of the catheter and the balloon was not retracted when the catheter was pulled out The degree of filling of the balloon was considered appropriate when the balloon became flattened against the wall of the vessel which could be observed on fluoroscopy

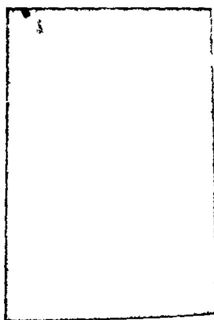
The main problem was leakage of the latex balloon This fact has been subjected to thorough investigation since it implies the obvious risk of uncontrolled embolisation of collapsed balloons

In a few cases a balloon was damaged during passage through the guiding catheter presumably due to adhesion of the balloon to the wall of the catheter and its penetration by the metal tube as the catheter was pushed forwards This could be avoided by flushing the balloon catheter through the guiding catheter

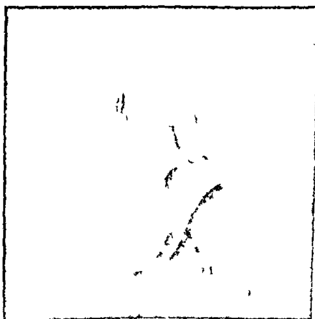
In several instances rupture of the balloon could be demonstrated after the balloon catheter had been withdrawn In most of the cases with leaking balloons the size of the balloons gradually decreased after detachment This slow or delayed leakage which may not be apparent until as long as one or two weeks later is probably caused by insufficiency of the neck of the balloon In vitro experiments suggested poor quality of the latex rubber to be one of the main factors causing leakage or rupture Thus in vitro experiments with balloons made of fresh latex subsequently demonstrated that all these balloons could be detached without leakage In some cases the solid neck of the balloon appeared to be too short and the distal part of the steel tube often proved to be thicker than intended This caused the manufacturer to make certain modifications of the balloons Thus the balloons are now made of fresh latex rubber solution and the solid neck of the balloons has been lengthened by 0 5 mm (from 0 5 to 1 0 mm) Also a thinner steel tube with an outer diameter of



a



b



c

Fig 2 a) Angiography of the common carotid artery in a pig (Subtraction) b) The balloon detached in one of the major branches of the external carotid artery c) Repeat angiography Occlusion has been obtained The balloon is indicated by the arrow (Subtraction)

shortly after the occlusion and repeat angiography from complications of anesthesia in the first case possibly enhanced by bleeding at the site of the arterial puncture In each of the remaining 2 pigs 2 balloons were introduced and detached In one case the balloons had not changed in size or position 4 weeks later and the vessels were still occluded In the second case the balloons had disappeared and repeat angiography demonstrated patent vessels at the site of the former occlusion

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ADVANCES IN THE DIAGNOSIS OF RENAL ANGIOMYOLIPOMA

D E APITZSCH O H WEGENER M KHALIL and R SÖRENSEN

Since the angiographic appearance of angiomyolipoma was first described by DOS SANTOS & WOHLWILL (1942) increased experience has shown that difficulties in distinguishing this benign tumour from a renal carcinoma are often encountered While some authors (VIAMONTE et coll 1966 KHILNANI et coll 1968 BARRILERO et coll 1974 BARRILERO 1977) are of the opinion that the benign tumour has special angiographic characteristics others such as KAUDE & CHANG (1970) emphasize the impossibility of excluding a renal carcinoma preoperatively For practical clinical purposes the angiography may occasionally allow a tentative diagnosis of a ha martoma However the vast majority of these tumours will be determined only after microscopic examination

The rare angiomyolipoma consists of individually differing zones of fat smooth muscle and angiomatous tissue In 50 to 80 per cent of cases it is detected as a lesion combined with tuberous sclerosis (Bourneville Pringle disease) belonging to the group of phacomatoses Frequently the tumour is bilateral total involvement of the kidneys is rare (KLAPPROTH et coll 1959 ANDERSON & TANNEN 1969 HEMMATI & THIELE 1970 APITZSCH & KALK 1974) Recognition of these tumours without con comitant tuberous sclerosis only occurs by chance (Case 2)

Up to the present time the radiologic diagnosis has been based upon conventional films of the kidney at urography and at nephroangiography

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less than 0 2 mm is used The new balloons have in in vitro tests proved to be considerably more reliable than those used in the present animal experiments

SUMMARY

A new catheter with detachable balloon for vascular occlusion was successfully used for permanent occlusion of the internal carotid artery as well as branches of the external carotid artery in 5 pigs The technique is intended for clinical use in man

ZUSAMMENFASSUNG

Ein neuer Katheter mit ablösbarem Ballon für die vaskuläre Okklusion wurde zur permanenten Okklusion der Arteria carotis interna sowie der Äste der Arteria carotis externa bei 5 Schweinen verwendet Es ist vorgesehen diese Technik für den klinischen Gebrauch beim Menschen zu verwenden

RESUME

Les auteurs ont utilisé avec succès un nouveau catheter a ballon largable pour les obstructions vasculaires utilisées pour l occlusion permanente de l artère carotide interne ainsi que pour les branches de l artère carotide externe sur 5 porcs Cette technique est destinée à l utilisation clinique chez l homme

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1 Hypervascular tumours with normal interlobar arteries (PALMISANO HARTEL et coll 1973 OWMAN 1973)

2 Macro and microaneurysms occasionally arranged in clusters (LOVE & FRANK 1965 VIAMONTE et coll KHILNANI et coll SEABURY et coll 1969 ISFORT & RINSCHE 1970 KAUDE & CHANG BIGOT et coll 1971 BRENDLER et coll 1971 DEININGER & TRAPP 1971 JÖRG 1971 MCCULLOUGH et coll 1971 CLARK & PALUBINSKAS 1972 BARRILERO et coll BARRILERO)

3 Onion skin in the venous phase (LOVE & FRANK LEMAITRE et coll 1968 MEANEY 1969 SEABURY et coll BRENDLER et coll DEININGER & TRAPP MCCULLOGH et coll SILBIGER & PETERSON 1971 CLARK & PALUBINSKAS)

4 Multiple cyst like regions in the parenchymal phase corresponding to the fatty part of the tumour (VIAMONTE et coll PALMISANO MEANEY SEABURY et coll BIGOT et coll HARTEL et coll OWMAN 1973)

5 Prolonged arterial phase and absence of arteriovenous shunts in spite of hyper vascularisation (JÖRG HARTEL et coll BARRILERO et coll OWMAN 1973 BARRILERO)

A differential diagnosis is impossible when the angiomyolipoma is hypovascular and without aneurysms and if a renal carcinoma has a similar vascularity to a hamartoma (MEISEL & APITZSCH 1978)

In the only case of renal carcinoma and hamartoma of the same kidney the malignant tumour could not be differentiated from the benign tumour even in retrospect (KAVANEY & FIELDING 1975)

Computer tomography provides possibilities to facilitate a preoperative diagnosis by its greater capacity for recording attenuation differences

Angiography and computer tomography have been performed in 2 cases of angiomyolipoma at this hospital As the appearances at computer tomography seem never to have been described before a brief report seems motivated

Case reports

Case 1 A 47 year old female was admitted because of sudden severe pain in the upper abdomen At the site of distress a mass was palpated At urography displacement of the right kidney pelvis towards the left side was demonstrated In the kidney region structure indicating renal tissue and fat appeared The origin of the space-occupying lesion could not be clearly identified At abdominal angiography and selective nephroangiography a large tumour in a duplicated kidney was demonstrated on the right side Several aneurysms were found some of them cluster like The nephrographic effect was very irregular The arterial phase appeared to be prolonged and no early draining veins were observed (Fig 2) The angiographic diagnosis was possible angiomyolipoma CT Large expanding lesion originating in the right kidney and with well demarcated fatty tissue Smooth borders to the surrounding area without any invasive growth into the adjacent organs No regional lymph node metastases

The angiographically suggested diagnosis of angiomyolipoma was confirmed by CT The attenuation values indicated fatty tissue in the right renal bed in the same area as observed



Fig 1



Fig 2

Fig 1 Intravenous urography Right renal pelvis (→) displaced towards the left side by a large expanding lesion with attenuation properties similar to fat Fused vertebrae of the lumbar spine

Fig 2 Same case as in Fig 1 Selective angiography *Double renal collecting system with* tumour in the larger part of the right kidney Multiple aneurysms some arranged in clusters The tumour region is still in the arterial phase while the rest of the kidney is in the parenchymal phase



Fig 3 Selective angiography Hypovascular tumour with neovascularity No cortical spur formation

Fig 3

An expanding lesion in the kidney in some regions with an attenuation similar to that of fat is characteristic (PALMISANO 1967 BARON et coll 1977) Such an appearance may, however also be observed in a lipoma (WINDHOLZ 1946) BARON et coll detected lipid regions in 5 of 6 angiomyolipomas retrospectively while 10 renal carcinomas did not have fatty regions microscopically

The angiographic characteristics of the angiomyolipoma as reported in the literature by different authors are as follows

icient to determine the true nature of the tumour Only by comparing the results the two methods could a definite diagnosis be made However further experience necessary for a clear evaluation of the value and accuracy of the diagnosis of renal giomyolipoma with combined CT and angiography

SUMMARY

Two cases of renal angiomyolipoma (benign hamartomas) are presented These rare nours were preoperatively diagnosed by comparing the conventional film angiography d computer tomography

ZUSAMMENFASSUNG

Zwei Falle von renalen Angiomyolipomen (benignen Hamartomen) werden vorgestellt denen der Vergleich von Abdomenleeraufnahme Angiographie and Computertomo aphie die praoperative Diagnose dieser seltenen Tumoren ermoglichte

RÉSUME

Les auteurs présentent deux cas d angiomyolipomes renaux (hamartomes bénins) la omparaison de la radiographie de l abdomen sans préparation de l angiographie et de la omodensitométrie a permis le diagnostic pré-operatoire de ces tumeurs rares

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Fig 4 Same case as in Figs 1 and 2 Computer tomography Fat containing mass on the right side A larger remainder of renal parenchyma (→) and small well demarcated remnants

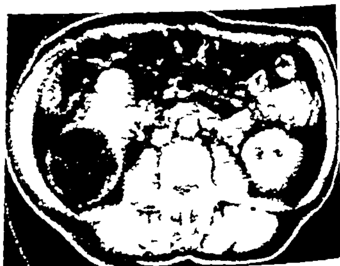


Fig 5 Same case as in Fig 3 Computer tomography Rounded mass in the tilted right kidney with attenuation values similar to fat Inconspicuous retroperitoneal structures

on the conventional abdominal film The diagnosis of an angiomyolipoma was confirmed at microscopy No abnormalities indicating tuberous sclerosis were found

Case 2 In a 65 year old female with chronic atheromatous vascular disease in both legs an abdominal aortography was performed As an incidental finding there was a hypovascular space occupying lesion in the lower pole of the right kidney (Fig 3) The patient had no history of renal disease The selective angiography demonstrated a hypovascular tumour with sparse neovascularity which was considered to be a renal carcinoma (Fig 5) No regions indicating fatty tissue

At CT a mass 5 cm × 6 cm with smooth borders to the parenchyma was detected Septal structures crossed the perirenal space The attenuation values indicated fatty tissue No enlarged regional lymph nodes

Diagnosis Fatty tumour of the right kidney without signs of malignancy possibly angiomyolipoma which was confirmed at microscopy No indication of tuberous sclerosis

Discussion The 2 cases well elucidate the diagnostic advantage achieved by CT In both cases one examination angiography or computer tomography was not

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PLACENTA SCINTIGRAPHY USING MARKERS OF THE UTERINE CERVIX AND PELVIC SKELETON

E HONORÉ and P B FREDERIKSEN

Placenta scintigraphy is a well established examination demonstrating the placenta in the form of a blood pool scintigram It provides no means of determining the position of the internal orifice of the cervix uteri Marking of palpable bony land marks has been employed in order to determine the site of the internal orifice but JOHNSON et coll (1972) have shown that the position of the orifice in relation to the skeleton varies Methods using loose markers in the vagina in order to indicate the site of the cervix have been described (JAMES et coll 1971 EDELING et coll 1976) ÅSARD et coll (1972) reported a technique in which the relationship between the marker and the cervix is constant this is ensured by the use of a guide tube fixed to the cervix by means of a tenaculum

This report describes an atraumatic marking of the uterine cervix and surface bony landmarks The scintigram enables calculation of the distance of the placental margin from the cervix markers

Method

The scintigraphy was performed with $^{99}Tc^{m}$ serum albumin which was produced in the department by a modification of the method described by MCAFFEE et coll (1964) Five hundred mg of potassium perchlorate were given by mouth prior to the scintigraphy in order to block the thyroid gland of both mother and foetus

The cervix markers were produced from a plastic vein catheter into which $^{99}Tc^{m}$ pertechnetate corresponding to 30 μCi was injected The catheter was then cut to a

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Table 1

Period of pregnancy at placenta scintigraphy

No of cases	Weeks of pregnancy
7	Before 28
25	28-32
52	32–36
17	36-40

Table 2

Diagnosis at $^{99}Tc^m$ placenta scintigraphy and method of birth in patients with clinically suggested placenta praecia

Diagnosis	No of cases	Caesarian section	Vaginal birth
Total placenta praevia	6	6	0
Marginal placenta praevia	12	5	7
No placenta praevia	83	12	71
Total	*101*	*23*	*78*

and the internal cervical os was designated as no praevia less than 5 cm but with the margin of the placenta not overlapping the marker as marginal placenta praevia (Fig 2) and when the placenta clearly covered the marker as total placenta praevia

In 6 patients total placenta praevia was diagnosed in 12 marginal placenta praevia and in the remaining 83 no praevia (Table 2)

The placenta was found to be at the site determined by the scintigraphy in all the 23 cases operated upon with Caesarian section

Four of the 5 patients with marginal placenta praevia who underwent Caesarian section had complications contributing to the indication for operation Four of the remaining 7 patients with marginal preaevia had a marginal detachment or placental impression commensurate with a low position of the placenta Complications arising from the abnormal site of the placenta did not occur in any of the patients giving birth via the vagina

Discussion

Scintigraphy of the placenta is considered to be safe for both mother and child inasmuch as it is atoxic and the amount of radiation is very small (FREDERIKSEN et coll 1969 VAN DER MERWE et coll 1970)

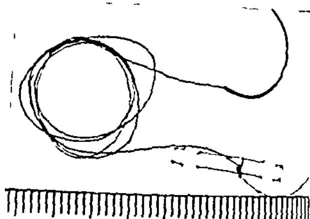


Fig 1 Cervix marker An 18 mm long welded plastic venous catheter containing 30 μCi of $^{99}Tc^m$ per technetate Catgut suture for fixation of the marker to the anterior fornix of the uterine cervix

length of 15 mm and closed by means of a plastic welding apparatus (Fig 1) At an ordinary gynaecologic inspection the marker was placed in the anterior fornix where it was fixed in position to the surface of the cervix using a catgut suture

The scintigram was produced using a gamma camera with diverging collimators, immediately after intravenous administration of 1 mCi of $^{99}Tc^m$ labelled human serum albumin An anterior scan was made first and thereafter a lateral one from the side on which the placenta was observed Additional external markers were used in the lateral scan of the upper edge of the symphysis and the spinous process of the 5th lumbar vertebra The distance between the markers was measured with a pelvimeter This was employed in the scintigram for calculating the reduction factor necessary in order to determine the correct distance between the placental margin and the cervix marker

Material and Results

The investigation was a prospective one and consisted of 101 patients all of them were admitted during a period of 20 months on a suggestion of placenta praevia The patients presented with vaginal bleeding or a high lying foetus Only patients who had passed the 25th week of pregnancy were included in the series

A satisfactory demonstration of the placenta and its distance from the marker was obtained in all the cases The majority of patients were examined between the 32nd and 36th weeks of pregnancy (Table I) In two cases where repeat scintigraphy was required the first scintigraphy was made before the 28th week

Scintigraphy was never carried out in an acute condition and at the earliest was made 5 days after cessation of the bleeding episode The attachment of the markers to the cervix did not provoke haemorrhage in any of the patients nor any other complications

A calculated distance of 5 cm or more between the lower margin of the placenta

atients 6 had total placenta praevia and 12 marginal placenta praevia No incorrect valuation of the scans or complications occurred The examination supplements ultrasound canning in late pregnancy

ZUSAMMENFASSUNG

Eine Methode fur die Placenta Szintigraphie wird beschrieben welche eine Differential Diagnose zwischen einer totalen und marginellen Placenta praevia ermoglicht Die Cervix uteri die Symphyse und der 5 Lendenwirbel werden bei der Szintigraphie in Form von atraumatischen Markierungen mit einbezogen Von 101 untersuchten Patienten hatten 6 eine totale Placenta praevia und 12 eine marginelle Placenta praevia Keine falschen szintigraphischen Diagnosen wurden gestellt und keine Komplikationen traten auf Die Untersuchung bildet eine Erganzung zur Ultraschall Untersuchung in der spaten Graviditat

RÉSUME

Description d une méthode de scintigraphie du placenta qui donne un diagnostic differentiel entre le placenta praevia total et marginal Le col uterin la symphyse et la 5 vertèbre lombaire sont inclus sur la scintigraphie au moyen de marqueurs atraumatiques Sur 101 malades examinées 6 avaient un placenta praevia total et 12 un placenta praevia marginal Il n y a pas eu d interprétation incorrecte des scintigraphies ni de complication L examen complète l échotomographie à la fin de la grossesse

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Fig 2 Marginal placenta praevia Distance between the outer markers 26 cm corresponding to 4 cm on the scintigram Distance of placenta from the cervix marker therefore 4 5 cm Vaginal birth with rupture one cm from the placental margin

The use of markers was desirable for reducing the uncertainty with regard to the relationship between the internal orifice of the cervix and the margin of the placenta which is known from experience to be a source of erroneous diagnosis (Niehoff et coll 1970 Egerno et coll 1971 Urbanek & Graf 1971) Previously one method has appeared allowing an exact localization of the internal cervical os (Åsard et coll) It has not been tried at this hospital but seems to have some disadvantages as being somewhat complicated and may involve a risk of bleeding in case of placenta praevia The method now presented is atraumatic, involves less risk of provoking a new bleeding and does not limit the mobility of the patient between the application of the marker and the end of the examination It makes possible a certain differentiation between total and marginal placenta praevia and thus improves the clinical reliability of the method No complications or incorrect evaluation of the scans of clinical importance occurred in the 101 patients

With ultrasound scanning it is possible to rapidly determine the localization of the placenta in the uterus as early as in the second trimester (Hollander 1971 Bang & Hasch 1976) In contrast to scintigraphy the ultrasound method is therefore well suited for screening of a large number of patients Cases of asymptomatic abnormality of the site of the placenta are now being diagnosed early in pregnancy relatively more often with this method and placenta praevia can be excluded in many patients in whom the clinical assessment would otherwise have suggested this condition However late in pregnancy a placenta praevia may be difficult to exclude by means of ultrasound examination if the placenta has a low attachment to the posterior wall of the uterus (Hollander Bang & Hasch) If this abnormal position cannot be excluded by means of ultrasound placenta scintigraphy should be added at the latest in the 37th week

SUMMARY

A method of placenta scintigraphy is described which provides a differential diagnosis between total and marginal placenta praevia The uterine cervix symphysis and 5th lumbar vertebra are included on the scintigram by means of atraumatic markers Of 101 examined

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QUANTITY OF TOMOGRAPHIC BLURRING

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Tomographic blurring has a qualitative and a quantitative aspect Good quality of blurring implies that every blurred contour has a perfectly smooth appearance to the eye so that no impression of contour sharpness is obtained within the zone of changing density limiting the blurred image The quantity of blurring on the other hand is related to the so called cut section thickness This term has no real back ground since what gives rise to sharp depiction in a tomogram is not a well defined layer with plane parallel limits in the object It has been shown from a theoretical aspect by REICHMANN (1972) as well as in practical experiments by ECKERDAL (1973) that the limitation of the tissue layer which gives rise to a sharp image has an irregular shape Nevertheless the term cut section thickness appears impossible to eradicate simply because there is need for some expression indicating the quantity of tomographic blurring

In an effort to optimise the quality of tomographic blurring ÅSTRAND & REICHMANN (1974) investigating different types of simulated spiral tomographic movements found that a nearly perfect tomographic blurring could be obtained by means of pirals with ten revolutions Later experiments have indicated (ÅSTRAND & REICHMANN unpublished results) that clinically acceptable results may be obtained by means of five or even four revolutions within the spiral However regardless of the number of revolutions every optimised spiral has a geometric shape where the spiral proceeds from the periphery to an end point rather near to the central point of the spiral system This means that if such a spiral is compared with a circular tomographic movement having the same tomographic angle the quantity of blurring must be less for the spiral than for the circle The reason for this is that in the former the

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QUANTITY OF TOMOGRAPHIC BLURRING

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focus partly travels near to the central point, which implies reduced blurring Th question thus arose to what extent the quantity of tomographic blurring is lost when a circle is replaced by an optimised spiral movement having the same maximum tomographic angle

Tomographic blurring can be mathematically expressed by means of Fourier analysis, the results being expressed as the transfer function (TF) or the modulation transfer function (MTF) This technique has been tested by HAUS et coll (1973) and HARDING & DAY (1976) The latter authors tried to optimise the quality of blurring in this way The general basis for this type of optimisation is given in Fig 1 indicati the TF for a circular tomographic movement with a given tomographic angle Th same diagram shows the TF for an optimised movement involving ten concentric circles (optimisation carried out according to ÅSTRAND & REICHMANN 1974) this movement path having the same angle as the single circle

The TF curves differ in two aspects They both start at the 100 per cent level and proceed down to the x axis Both curves cross the x axis and continue in a series of waves to the right of the primary zero point For the circular movement these waves are more numerous and of greater amplitude than for the composite movement Th waves indicate imperfections in the tomographic blurring diminishing blurring quality HARDING & DAY optimised the quality of blurring in an analysis of these waves to the right of the primary zero point In the optimised movement the waves have been removed as completely as possible The second aspect where these tw curves differ is the location of the primary zero point For the optimised concentri circle movement this point is clearly to the right of that of the simple circular move ment despite identical tomographic angles Since the part of the TF curve situated t the left of the primary zero point describes the true tomographic depiction it may b assumed that the difference in this respect reflects a difference in blurring quantit This hypothesis has been tested for a series of tomographic movements

Material and Methods

A number of tomographic movement paths all having a tomographic angle of 2(were tested with regard to the quantity of blurring Spirals were simulated by co centric circles Since there are two ways of affecting the blurring quantity in a spiral, two sets of simulated spiral motions were investigated The first way of changing the quantity of blurring implies a change in the geometry of the spiral If a spiral has all its revolutions located in the periphery the blurring will be greater than if the mo ment path extends towards the centre The second alternative for changing the quantity of blurring implies a spiral with constant geometry However if the dose rate is assumed to be variable a relatively large fraction of the total dose may be emitted when the tube is in the periphery of the spiral yielding high quantity of blurring A low blurring quantity is obtained if most of the total dose is delivered when the focus is near to the centre These mechanisms for affecting the quantity of

Table

Data for the simulated spirals

Constant dose rate				Constant geometry			
Revolution	Radius			Revolution	Radius	Dose	
	1	2	3			4	5
	1 000	1 000	1 000	1	1 000	0 100	0 056
	0 945	0 860	0 780	2	0 895	0 200	0 065
	0 890	0 770	0 555	3	0 790	0 250	0 070
	0 835	0 585	0 335	4	0 685	0 200	0 091
	0 780	0 445	0 110	5	0 580	0 100	0 121
				6	0 475	0 050	0 137
				7	0 370	0 040	0 160
				8	0 265	0 030	0 167
				9	0 160	0 020	0 100
				10	0 055	0 010	0 033

tomographic blurring were tested in simulated spiral systems The data concerning the different tomographic movements are listed in the Table For these tomographic movements the TF was calculated according to HARDING & DAY Simultaneously the TF for circular tomographic movements with different tomographic angles was calculated The aim was to find out which circular movement gave rise to the same TF curve to the left of the primary zero point as did each simulated spiral

The quantity of blurring for each simulated spiral was tested by means of tomography of a slanted plexiglass plate where equidistant metal wires had been inserted The tomographic plane was adjusted so as to coincide with one of the wires The other wires being parallel to this reference wire were situated at constantly increasing distances from the tomographic plane in both directions Tomography was carried out in a Polytome using non screen industrial film (Kodak Industrex C) placed in a metal cassette without intensifying screens Nominal focus size was 0 6 mm × 0 6 mm In the image obtained the depiction of the different wires displayed the quantity of blurring so that with low blurring quantity more wires were sharply depicted than with high The simulated spirals (Table) were compared with circular movements performed at different tomographic angles starting at 20 being lowered in steps of 1 to values giving rise to blurring quantities visibly smaller than that of the simulated spirals tested Subsequently the different images obtained by simulated spirals were compared with the simple circular images displaying the same quantity of blurring i e the same progression of unsharpness in both directions from the reference metal wire

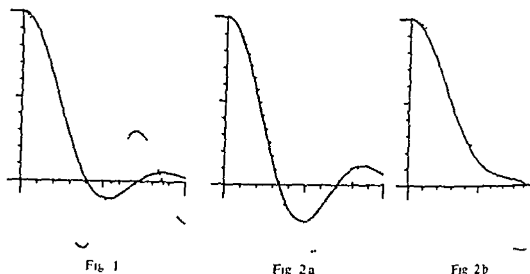


Fig 1 Transfer function of an optimised spiral (——) and a circle ( ) having the same maximum tomographic angle To the right of the first zero point the function of the circular tomographic movement displays a series of oscillations implying a diminished quality of blurring The first zero point of the spiral occurs at a higher spatial frequency than that of the circle suggesting a lower quantity of blurring

Fig 2 Transfer function of spiral ( ) as compared with circular ( ) movements chosen so as to yield a curve of the same shape to the left of the first zero point The spirals are those having 10 revolutions listed in the Table with a tomographic angle of 20 The one with most of the radiation dose located in the periphery of the spiral is compared with a circle of 14 (a) while the spiral where most of the dose was delivered near to the centre is compared with a circle of 9 (b)

Results

Excellent agreement was obtained between calculated data as to blurring quantity and experimental results One series is presented in Fig 2 which demonstrates the simulated spiral of constant geometry with distribution of the dose rate within the spiral In (a) the TF for a simulated spiral with a high quantity of blurring is shown The curve coincides closely with a circular tomographic movement having a tomographic angle of 14 For the second modification of the simulated spiral the TF curve did not have exactly the same form as for any circular movement (b) most closely resembling the TF for a circular movement of 9 In Fig 3 the tomographic images obtained by these movements are presented For the other simulated spirals tested similar results were obtained

Discussion

A way to express the quantity of tomographic blurring has always been desired Generally, the concept of thickness of the tomographic layer has been used although it has been demonstrated beyond doubt that a plane parallel layer does not exist The main factor leading to variable section thickness is the *interplay between contrast and sharpness* which is well known in every type of radiographic depiction If the unsharpness is high it can to a certain degree be compensated for by high contrast

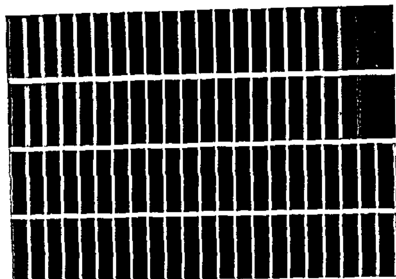


Fig 3 Tomograms of a slanted disc of plexiglass with equidistant metal wires The tomographic movements analysed in Fig 2 were used viz (from above) spiral 0 main dose peripherally circle 14 spiral 0 main dose centrally circle 9 As expected from the transfer functions (Fig 2) the quantity of blurring is the same in the 2 former and the 2 latter respectively A clear difference in blurring quality between the wires in spiral 0 and circle 14 exists blurring being smoother in spiral 0 movement

In this way structures with high attenuation differences may be demonstrated in a tomogram even if they are situated relatively far from the tomographic plane (REICHMANN ECKERDAL) The transfer function expresses this interplay between contrast and unsharpness and may thus be expected to be the ideal mathematical expression for the quantity of tomographic blurring For practical clinical purposes the quantity of blurring for different spiral systems may be correlated to the blurring quantity inherent in circular systems with a smaller tomographic angle giving rise to the same transfer function

SUMMARY

A spiral tomographic movement gives rise to a lower quantity of blurring than does a circular movement with the same tomographic angle since in the former the focus comes nearer to the central point It has been demonstrated that the transfer function may be used to express the quantity of blurring for different tomographic movements For the sake of convenience the blurring quantity for every type of spiral movement may be expressed in terms of the tomographic angle of a circular movement giving rise to the same transfer function

ZUSAMMENFASSUNG

Eine spiralenformige tomographische Bewegung gibt zu einer niedrigeren Quantitat von Verzerrung Anlass als eine zirkulare Bewegung mit dem gleichen tomographischen Winkel

da im ersten Fall der Fokus näher an den Zentralpunkt kommt Es wurde nachgewiesen, dass die Transfer Funktion verwendet werden kann um die Quantität der Verzerrung bei verschiedenen tomographischen Bewegungen auszudrucken Aus Grunden der Einfachheit, kann die Quantität der Verzerrung fur jeden Typ einer spiralformigen Bewegung in Termen eines tomographischen Winkels einer zirkularen Bewegung ausgedruckt werden die zu gleichen Transfer Funktion fuhrt

RESUMÉ

Un mouvement tomographique spiral donne une moindre quantité d effacement qu un mouvement circulaire ayant le même angle tomographique car dans le mouvement spiral le foyer s approche davantage du point central Il a été démontré que la fonction de tra fe peut être utilisée pour exprimer la quantité d effacement pour différents mouvements tomographiques Pour des raisons de commodité la quantité d effacement de n importe quel type de mouvement spiral peut être exprimée sous la forme de l angle tomographique d un mouvement circulaire donnant la même fonction de transfert

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ENERGY IMPARTED IN ROENTGEN DIAGNOSTIC PROCEDURES

Results of two surveys during the periods 1958–1960 and 1974–1976 related to technical modifications

MONICA GUSTAFSSON

In many countries the largest artificial contribution to the irradiation of the population is derived from diagnostic radiology In Sweden this is approximately equal to the natural irradiation (BENGTSSON et coll 1977) The importance of optimizing the patient exposure is being increasingly stressed by national and international authorities (ICRP 1970 1973 1977 the Swedish National Board of Health and Welfare 1976) as well as by the individuals concerned (ELLIS 1977 EVANS 1977) Trends in the genetically significant dose in Sweden the Netherlands the United Kingdom and USA (KOEN & WEBER 1973 FITZGERALD & WHITE 1975 VILLFORTH 1975 BENGTSSON et coll) show that the increase in examination frequency has not been compensated for sufficiently by a reduction of the dose per examination

From 1958 to 1960 CARLSSON performed an extensive investigation (here called the 1960 data) of the energy imparted (integral dose) during several diagnostic radiographic procedures (CARLSSON 1965 b) Among other results he demonstrated that a dose reduction was achieved when standard film was replaced by rapid film Since then many important technical modifications have taken place several of them are expected to result in a reduction of the patient irradiation From a repeat survey in

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Table 1

Irradiation of the Swedish population from some diagnostic radiographic procedures (BENGTSSON *et coll* 1977)

Examination	Percentage contribution to		
	Energy imparted	Mean bone marrow dose	Mammary dose
Gastrointestinal tract	27	32	7
Spine hip pelvis	21	25	9
Chest full size	6	6	17
Urography	16	6	24
Total	70	69	57

1974 to 1976 (here called the 1975 survey) at the Department of Diagnostic Radiology at the University Hospital in Lund where the technical changes were known the total effect on patient irradiation could be demonstrated The energy imparted is then a good measure since it is less variable than the individual organ doses (BENGTSSON et coll)

A few comparisons of patient irradiation with different techniques have been presented (SCHOLN 1966 CHIBA 1968 LÖHR et coll 1977) all dealing only with fluoroscopy by the old conventional method and by image intensifier television chains The first measurements in the present investigation were carried out during examinations of the gastrointestinal tract including fluoroscopy (GUSTAFSSON 1975) Later urography full size radiography of the chest and skeletal radiography were also included (GUSTAFSSON 1977)

Materials and Methods

Measurements were taken from approximately 600 diagnostic procedures at the University Hospital in Lund The choice of examinations was arranged to include those of greatest importance for the irradiation of the Swedish population as a whole (cf Table 1 calculated from BENGTSSON et coll)

For every procedure at least two examination rooms with different technical equipment were employed Image intensifier TV systems were included in fluoroscopy for all cases Different screen film systems were used requiring from about 0 1 μC kg^{-1} (0 4 mR) to about 0 2 μC kg^{-1} (0 8 mR) for a net blackening of 0 9 In all but one examination room CEA Wicor X RP film was used Examination rooms with and without automatic exposure control and brightness stabilization were also included

In all measuring situations except one the total filtration of the radiation unit was checked by measurement of the first half value layer at one high tension value If

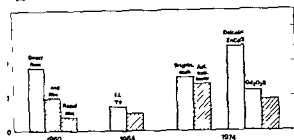


Fig 1 Energy imparted at stomach examinations 1960 to 1974 [ ] Fluoroscopy [hatched] radiography

n ideal geometry could not be achieved the extrapolation method according to TROUT et coll (1960) was applied The filtration was calculated from tabulations by MIKA & REISS (1973) For a given tube used in fluoroscopy and radiography the filtration was checked for both types of examinations Variations in calculated in ierent filtration due to the different wave forms as pointed out by REINSMA (1960) were observed The peak potentials in the various units were measured by a penetra neter (manufactured by G E C Medical Equipment Ltd) according to a description by ARDRAN & CROOKS (1968)

The energy imparted was calculated from the areal exposure according to CARLSSON (1963) The areal exposure was measured by transparent plane parallel ionization chambers (manufactured by Physikalisch Technische Werkstatten) attached to the secondary diaphragms of the tubes The ionization current charges a condensor which is read off by an electrometer and subsequently discharged

Up to three ionization chambers were connected in parallel to the electrometer at the same time The contributions from fluoroscopy and radiography were derived separately by connecting a recorder

Calibration of the ionization chambers in units of R cm²/V was performed in air under the applied radiation qualities and as a rule in the actual geometry This was always the case when an examination couch was located between the measuring chamber and the patient The monitors were calibrated against ionization chambers whose calibrations are in turn traceable to the National Swedish Radiation Standards Laboratory and the Rijks Instituut voor de Volksgezondheid Bilthoven the Netherlands

Results

The energy imparted to individual patients varies considerably even though all measurements are performed in the same hospital The distribution of patient doses normally includes a few extremely high values and the distribution may be log normal (KOEN & WEBER GURSKY 1974) The relation between mean and median values indicates how skew the distribution is For comparisons the median values are most appropriate (GURSKY) and consequently discussed in the present report Measure

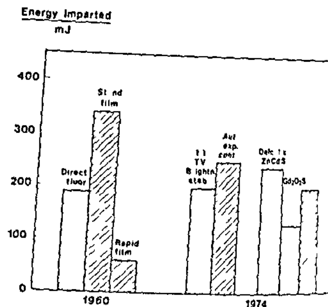


Fig 2 Energy imparted at barium enema 1960 and 1974 Fluoroscopy radiography

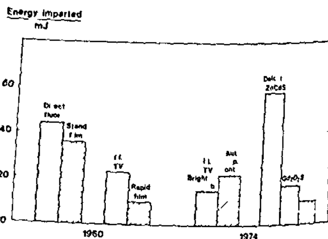


Fig 3 Energy imparted at cholecystography 1960 and 1974 Fluoroscopy radiography

ments during examinations performed by medical students were excluded since no such measurements were included in the 1960 investigation

The conversion from areal exposure to energy imparted according to CARLSSON (1963) involves some approximations the energy imparted is for example always calculated for a 200 mm thick water layer The accuracy of the method is given by CARLSSON (1965 a)

Gastrointestinal tract Measurements were performed in 3 examination rooms during 270 procedures 160 of which were included in the comparison (examinations performed by medical students and examinations with new techniques such as double contrast were excluded) Results from stomach and colon examinations and cholecystography, are given in Figs 1 to 3 The median values of the total energy imparted (10 mJ = 1 kg rad) from fluoroscopy and radiography are compared with

Table 2

Average fluoroscopy time and average number of films exposed per examination in 1960 and 1975

Examination	Average fluoroscopy time (min)		Average number of films	
	1960	1975	1960	1975
Stomach	7 4	6 0	10	11
Barium enema	5 3	4 2	9 1	8 7
Cholecystography	2 8	1 9	5 0	5 2
Chest full size			3 4	2 3
Urography			13	12

the results from CARLSSON (1965 b) and CARLSSON & KAUDE (1967) as cited by HOLM & KAUDE (1968)

The introduction of rapid film in 1960 resulted in the expected dose reduction The decrease was confirmed by measurements from stomach examinations in 1964 (CARLSSON & KAUDE 1967) In 1974 however the energy imparted from radiography has increased considerably In all the three examination types the increase is most marked with automatic exposure control

A few measurements from fluoroscopy with an image intensifier TV chain were recorded in 1960 and showed a decrease which was also manifest in 1964 In stomach and colon examinations the energy imparted from fluoroscopy with or without automatic brightness stabilization is the same or even higher in 1974 than with direct fluoroscopy in 1960 In cholecystography a decrease is observed except with the Delcalix system whose high noise level makes it very unsuitable for fluoroscopy on such low contrast objects The introduction of a gadolinium oxysulphide screen reduced the dose by 50 per cent or more The mean value of the energy imparted from fluoroscopy and radiography is between 1 0 and 1 4 of the median value except for radiography in stomach examinations and cholecystography where the mean energy imparted is 1 5 to 2 0 of the median value Such skew distributions were not reported by CARLSSON (1965 b)

The fluoroscopy time was generally shorter with the image intensifier TV systems (Table 2) Even if the values presented are crude estimates due to the large variations a clear tendency exists This reduction may result from the shorter time of recognition in an image with improved resolution SCHOEN and CHIBA failed to observe any difference in fluoroscopy time of stomach examinations with direct fluoroscopy and image intensifier TV systems However LÖHR et coll detected a general increase in fluoroscopy time in examinations of the gastrointestinal tract according to the assumptions made by STIEVE (1970 1976) The increase in fluoroscopy time over a period of one week observed by LÖHR et coll could not be confirmed in the present

Table 3

Energy imparted during various examinations in 1960 (standard film) and in 1975 (RP film)

Examination	1960			1975		
	No of patients	Energy imparted (mJ)		No of patients	Energy imparted (mJ)	
		Mean	Median		Mean	Median
Chest full size	249	53	46	186	6 6	57
Urography	62	240	210	60	350	250
Spine hip pelvis	31	180	160	114	51	34

Table 4

Energy imparted in full size chest radiography in 1960 and 1975

Procedure	Year	No of patients	Energy imparted (mJ)	
			Mean	Median
Fluoroscopy	1960	286	26	23
Radiography				
Standard film	1960	249	26	23
Rapid film	1960	37	8 1	6 0
RP film	1975	186	6 6	5 7

material since too few measurements were recorded during each procedure daily and since too many physicians were involved

The average number of films exposed is almost the same in 1960 and 1974 Thus the automatic exposure control has probably not led to any decrease in the number of re takes

Full size chest radiography Median and mean values of the energy imparted in 1960 and 1975 are given in Tables 3 and 4 Since fluoroscopy is no longer used in routine examinations there is a substantial reduction of the total energy imparted Radiography with RP film in 1975 gives almost the same energy imparted as by rapid film in 1960 (Table 4) although the number of films exposed has decreased (Table 2) All the three examination rooms used in 1975 had automatic exposure control

Urography In urography the energy imparted has increased although the number of films exposed per examination has decreased (Tables 2 and 3) In 1975 the mean energy imparted was 40 per cent higher than the median value which indicates a relatively skew distribution with a few extremely high values (maximum value 1 700 mJ = 170 kg rad) In the examination room with automatic exposure control the number of films exposed was 10 per cent less than in the other room

Table 5

Energy imparted in Swedish diagnostic radiology during 1975 Min and max values indicate the lowest and highest hospital mean values in the survey conducted by the National Institute of Radiation Protection (NIRP)

Examination	Energy imparted (mJ)				
	NIRP 1974			Present material	
	Mean	Min	Max	Mean	Median
Stomach	310	90	460	360	300
Barium enema	600	380	940	440	420
Cholecystography	91	41	97	56	41
Chest full size	21	13	28	6 6	5 7
Urography	510	360	590	350	250

Spine hip and pelvis Relatively few measurements were performed during skeletal radiography in 1960 It is however clear that the energy imparted per examination has decreased appreciably The average values for 1960 and 1975 (Table 3) do not include the same proportion of the different procedures which lead to an overestimation of the decrease in the energy imparted The average decrease calculated from estimates on identical types of examinations is approximately 50 per cent Since there were relatively few examinations of each type in 1960 it was irrelevant to derive the number of films exposed per examination but a tendency for an increased number of films in 1975 is evident No definite difference was found between the number of films used in examinations carried out with and without automatic exposure control

Comparison with previous surveys Even if the main purpose was to examine the change in patient dose due to technical modifications a comparison of the results with other surveys is also of some interest particularly with the survey performed by the National Swedish Institute of Radiation Protection (NIRP) during 1974 (BENGTSSON et coll) In Table 5 the mean and median values recorded at the University Hospital in Lund are compared with the mean values estimated for the whole of Sweden as well as maximum and minimum hospital mean values It is obvious that results in Lund correspond to observations from other Swedish hospitals where the patient irradiation is low

Energy imparted or areal exposure for different examinations have also been reported by CHIBA SCHOEN GURSKY TELICHKO et coll (1974) SOBOL (1975) and LÖHR et coll GURSKY SCHOEN and SOBOL present values comparable to the Swedish mean values whil CHIBA reports very low areal exposure values LÖHR et coll and TELICHKO et coll quote significantly higher values Since these reports do not include description of all the technical data and the methods of calculating the energy imparted may differ no attempt will be made here to analyse the reasons for the discrepancies

Discussion

Initially the prime reason for the present investigation was the need to examine the expected reduction of patient irradiation after the introduction of rapid film in sensitive screens and image intensifier TV systems In the beginning no decrease in patient irradiation was found which motivated further investigation of the important examination types for the irradiation of the population It was also quite obvious that each factor of importance for the dose per examination had to be analysed

Three important factors in the accomplishment of the examination are the number of films or time of exposure beam limitation and compression of the patient The first one is illustrated in Table 2 No general tendency was found in the number of films exposed per examination with or without automatic exposure control The possible reduction of re takes due to the introduction of automatic exposure control (BERRY & OLIVER 1976 MCKINLAY & MCCAULEY 1977) is too small to be considered

No attempts were made either in the 1960 or the 1975 survey to quantify the compression of the patient Changes in beam sizes between the surveys could be observed on exposed films but since very few films from 1958 to 1960 have been saved no efforts were made to make a general comparison In fluoroscopy an analysis of the energy imparted the exposure data and the quotient of areal exposure and fluoroscopy time in 1960 and 1974 indicate that the fluoroscopy field area is about the same or somewhat larger in 1974 than in 1960 FRIK (1964) implied that the smaller entrance field of the image intensifier TV system compared to the direct fluoroscopy screen should induce the examiner to use a smaller field The higher quality of the image intensifier TV image could however lead to a less careful beam restriction It could be assumed that the image quality in direct fluoroscopy required careful beam limiting and compression of the patient to minimize the amount of scattered radiation

The technical factors of importance for the irradiation of the patient are somewhat easier to define and quantify The following account discusses the factors considered and the assumptions made in the subsequent analysis of expected and measured changes in the energy imparted in different examinations from 1960 to 1975 A detailed description of the technical equipment is excluded

Radiation quality The higher the tube potential and the more efficient the beam filtration the lower will be the energy imparted for a constant exit exposure The quantification of this energy dependence was based on depth dose data presented by TROUT et coll (1952 1963) and WACHSMANN & DIMOTSIS (1957) It was shown that for a 200 mm thick water layer the percentage difference in energy imparted for different half value layers is approximately half the percentage difference in depth dose at 200 mm depth

CARLSSON (1962) presented the variation of integral dose and skin dose with high tension for a constant exposure to the cassette and ARDRAN & CROOKS (1962) gave

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Grid absorption In all examinations a grid was used to reduce the influence of cattered radiation on the image The use of grids implies an increased dose to the atient The enhancement is characterized by the dose increment factor (bucky actor) which is the inverse of the total transmission A grid is most often identified y the grid ratio strip density (in numbers per cm) and focal distance However the ad content (expressed for example in mg cm^{-2}) is more significant for the grid quality as well as for the dose increment factor (BONENKAMP & HONDIUS BOLDINGH 959 HONDIUS BOLDINGH 1961 b STRID 1976)

The intermediate material is also of importance The dose increment factors for Lysholm grids with aluminium spacing are higher than for grids with the same lead ontent but with presspan as interspace material Disregarding the latter condition he dose increment factor increases with decreasing high tension and increasing lead ontent The contrast improvement factor also rises with increasing grid lead content HONDIUS BOLDINGH 1961 a)

In 1960 all grids used had the ratio 6 5 but no other characteristics were mentioned by CARLSSON In 1975 grids with a ratio from 7 to 12 with strip densities from 24 to 44 lines cm^{-1} and made by different manufacturers were used With the collaboration of the grid suppliers (RASMUSSEN 1976 LASER 1976) the lead contents of grids used in 1975 were estimated with relatively good confidence and an approximate estimate could also be derived for the grids used in 1960

Dose increment factors for various grids in use today have been measured by NIELSEN (1976) according to a method described earlier (NIELSEN 1973) The dose increment factors are given for different high tension values for a 200 *mm thick* water layer and with an entrance field size of 300 mm 300 mm Since the dose increment factor is a function of the field size (as well as the object *thickness*) the results quoted by NIELSEN (1976) may overestimate the dose increment to the patient However for comparisons between different examination rooms they should be adequate

A few grids were checked with reference to the total transmission in an arrangement with 200 mm polymethylmetacrylate irradiated by a 200 *mm* 200 mm field at 70 kV and 100 kV The transmission with and without grid was measured by a plane parallel ionization chamber (PTW DAI *Physikalisch* Technische Werkstätten) mounted approximately 50 mm behind the phantom The maximum and

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Table 6

Relative energy imparted per exposed film or unit time of fluoroscopy in 1975 calculated from measurements in 1960 and with regard to technical modifications in the interim (range covers different examination rooms)

Examination	Tension filtration	Grid absorption	Screen sensitivity	Film sensitivity	Abs in aut exp ioniz chamber	Abs in exam couch	Total
Gastrointestinal tract	0 9–1 0	1 0–1 7	0 3–0 8	0 4–1 0	1 1	—	0 2–0 9
Chest full size	0 7–1 0	1 1–1 6	0 3–0 5	0 4–0 6	1 0–1 1	—	0 2–0 7
Urography	1 . 1 3	1 0–1 4	0 4–0 8	0 4	1 0–1 2	0 9–1 0	0 3–0 5
Spine hip pelvis	1 1–1 2	1 4–1 5	0 4	0 4	1 0–1 1	0 9–1 0	0 3

30 μR s^{-1} (8 nC kg^{-1}s^{-1}) in the two examination rooms with automatic brightness stabilization (ZnCdS screens) The sensitivity at image intensifier TV fluoroscopy in 1975 would thus be about 3 3 times higher than with direct fluoroscopy in 1960 This corresponds to the reduction of energy imparted during fluoroscopy observed by CARLSSON & KAUDE as cited by HOLM & KAUDE

Distance patient—image intensifier In direct fluoroscopy the low luminous intensity of the screen forced the physician to minimize the distance between the patient and th screen This is no longer the case with the use of image intensifiers however the risk for an increased distance was put forward by STIEVE (1970) With the use of automatic brightness stabilization the examiner is unaware of the increase in patient exposure When the image intensifier is removed from the patient the screen exposure rate decreases due to the inverse square law but also and to a greater extent due to decrease in s attered radiation reaching the screen STIEVE (1970) demonstrated an increase in patient exposure by 10 46 and 73 per cent when the distance between the patient and the image intensifier was extended from 50 to 100 150 and 200 mm respectively

TROUT et coll (1975) measured a decrease in scattered radiation of 53 per cent with a 100 mm air gap and of 80 per cent with a 150 mm air gap From RAO et coll (1973) a decrease of 73 per cent with a 170 mm air gap can be calculated Estimates of th decrease in screen exposure with these data for the actual focus distances and with regard to grid absorption (no grids were used in the experiments mentioned) yield values in agreement with those of STIEVE (1970) This increase in patient dose will also occur in radiography with spot film device

Absorption in the automatic exposure monitor and the couch top The ionization chamber for automatic exposure control is usually placed between the grid and the cassette Such an arrangement causes an increased patient irradiation due to the at

minimum sensitivity of the chamber differ by less than 10 per cent at the energies used. The results agreed with the observations by NIELSEN (1976) considering the reduced scattered radiation due to the smaller radiation field (REISS & STEINLE 197[illegible]).

The grid ratio is the factor which determines the additional loss of primary radiation due to lateral and distance decentering and angulation error. The losses are directly proportional to the ratio. The majority of the grids used in 1975 had ratio [illegible] which, when compared with ratio 6.5 used in 1960, meant that the loss of primary radiation with the same grid errors, such as the unavoidable decentering in the Potter-Bucky grid, was almost doubled in 1975. The possible additional loss of primary radiation and the resulting decrease in total transmission was calculated for the different examination units.

Screen sensitivity. In 1960 par speed ($CaWO_4$) intensifying screens were used. These require an exposure of about 0.3 μC kg^{-1} (1 mR) to produce a net density of 0.9 on an ordinary film today (HOLJE & SVAHN 1974). In 1975 most of the examinations were performed with high speed screens requiring about half the exposure. Both calcium tungstate ($CaWO_4$) and barium sulphate ($BaSO_4$) screens were used.

The screen sensitivities, expressed as exposure to the cassette to produce a net film density of 0.9, as measured by HOLJE & SVAHN were adopted in the calculations. They also analysed the sensitivity as a function of high tension in $CaWO_4$ and $BaSO_4$ screens (with 200 mm polymethylmetacrylate and a grid with ratio 10 between the tube and the cassette containing two screens). Their results are in fairly good agreement with the measurements by WIDENMANN (1957) and by ARDRAN & CROOKS (1962) for comparable screens. The sensitivity of $CaWO_4$ screens has a broad maximum around 100 kV, while the sensitivity at 60 kV and 140 kV is approximately 13 per cent lower. The variation in sensitivity with high tension is more marked with $BaSO_4$ screens, especially at low potentials. A 25 per cent higher exposure is needed at 60 kV than at 95 kV to give the same film blackening.

Film sensitivity. During the 1960 survey standard film was mainly used but some measurements were also performed after the introduction of rapid film. CARLSSON (1965 b) stated that the exposure time with rapid film was reduced by a factor 2.6 and according to HOLM & KAUDE the cassette exposure declined from 2.5 mR (0.65 μC kg^{-1}) to 1 mR (0.26 μC kg^{-1}). An exposure of approximately 0.3 μC kg^{-1} is needed to produce a net density of 0.9 on the film used in the 1975 survey (CEA Wicor X RP) with identical screens used in 1960 (HOLJE & SVAHN). Hence it may be concluded that the sensitivity of the RP film as developed in this hospital is not much different from the sensitivity of the rapid film introduced in 1960.

Sensitivity of the fluoroscopy screen. Direct fluoroscopy with a ZnCdS screen was performed in 1960. According to STIEVE (1970) the exposure rate needed on these screens was 100 μR s^{-1} (26 nC $kg^{-1}s^{-1}$). In 1975 the frequent exposure rate was

Table 8

Measured energy imparted per exposed film in 1975 relative to the value derived from the 1960 data and technical changes in the interim Minimum and maximum ratios indicated

Chest full size	1 4-2 8
Urography	3 7-4 2
Spine hip pelvis	0 9-1 7

could also be questioned whether the number of measurements are not too few in some cases but for all comparisons the median values are used and the general trend should be applicable

The calculated relative energy imparted per exposed film or unit time of fluoroscopy is given in Table 6 (range covers different examination rooms) together with the influence of different factors The calculations for fluoroscopy are not included The possible increases in dose due to increased distance between patient and image intensifier or spot film device grid decentering and grid angulation error are not given The measured values in 1975 are compared with those calculated in Table 7 and 8

Examinations of the gastrointestinal tract The radiation quality has not changed appreciably since 1960 (Table 6) The grids have become more effective and have ratios of 8 or 12 compared with 6 5 in 1960 This increases the risk for additional attenuation due to grid errors Screen sensitivities have improved and also the film sensitivity compared with standard film in 1960 All examination rooms had an automatic exposure ionization chamber mounted The lowest total decrease of 10 per cent was derived for the examination room with the least sensitive recording system in 1975 compared with examinations with rapid film in 1960 For the rest the dose absorbed in radiography should be 80 per cent lower in 1975 than in 1960

In fluoroscopy the calculated decrease of energy imparted per unit time is approximately 60 per cent

From previous results it is obvious that *the expected dose reductions have not occurred* Ratios of measured and calculated values are given in Table 7 With the exception of cholecystography manually exposed the difference is substantial Fluoroscopy with the Delcalix system is not included since corresponding image quality was not comparable to the other systems

One possible reason for the elevated dose values is an increased distance between the patient and the image intensifier or spot film device An extra separation of 100 to 150 mm (not an unrealistic assumption according to HOLM 1977) means a 65 per cent increase in patient irradiation due to the inverse square law and a reduction in scattered radiation a 5 to 10 per cent increase due to grid defocussing and even

Table 7

Measured energy imparted per exposed film or unit time of fluoroscopy in 1975 relative to the value derived from the 1960 data and technical changes in the interim period

Examination	Radiography		Fluoroscopy with aut brightness stab
	With aut exp contr	No aut exp contr	
Barium enema	5 2	3 3	3 5
Stomach	4 4	3 0	2 7
Cholecystography	3 8	1 3	2 7

tenuation in the monitor itself This attenuation was checked for two ionization chambers delivered by Siemens AG and two ionization chambers used in Philips units 200 mm polymethylmetacrylate simulated the patient, a secondary radiation grid was used and a plane parallel ionization chamber (PTW DA1) measured the exposure behind the ionization chamber A second plane parallel ionization chamber attached to the secondary diaphragm served as monitor The decrease in exposure was measured in the Siemens units as 16 per cent at 70 kV and as 7 per cent at 100 kV The figures for the Philips units were 21 per cent at 70 kV and 11 per cent at 100 kV

In examinations performed by an overcouch tube the couch top reduces the exposure to the image recording medium and thereby increases the dose to the patient In 1960 all couch tops were made of wood, but at present some units are laminated with plastic assumed to enhance the radiation attenuation The absorption was checked on three couch tops representative for the units included in the 1975 survey To simulate the radiation quality behind the patient the total filtration of the beam was adjusted to approximately 22 mm Al (ICRU 1963) The decrease in exposure was measured by a transparent plane parallel ionization chamber registering the areal exposure above and beneath the couch A similar ionization chamber mounted on the secondary diaphragm served as monitor All Siemens units with a wooden couch top decreased the exposure by approximately 14 per cent (at 70 kV and 100 kV) The Philips wooden couch top caused a decrease of about 8 per cent and the plastic one about 15 per cent of the incident radiation

Comparison of the calculated and the measured energy imparted in 1975 After the influence of the different technical factors on the energy imparted to the patient has been quantified it should be possible to calculate an expected energy imparted in 1975 from the 1960 data by CARLSSON (1965 b) and the changes known since then This estimation must be based upon the energy imparted per film exposed or per unit time of fluoroscopy However the calculation is subject to uncertainties regarding for example the grid characteristics in 1960 and the advances in film sensitivity It

Urography The radiation quality has been changed since 1960 leading to an increased energy imparted (Table 6) This is due to lowering of the high tension from 90 kV to 70 kV together with a decrease in primary filtration from approximately 3 7 mm Al to approximately 2 4 mm Al This change in radiation quality will also influence the grid absorption screen sensitivity (especially in the unit where $BaSO_4$ screens are used) and the absorption in the ionization chamber Grids with ratio 7 and 12 were used in 1975

The total reduction in the energy imparted per exposed film was calculated to approximately 60 per cent but instead a 25 to 75 per cent increase was registered i e about four times higher than expected (Table 8) This great difference cannot be explain d in terms of factors such as the additional absorption due to angulation error of a grid with higher ratio or by uncertainties in the present calculations

The discrepancy b tween calculated and measured energy imparted must be due to some modification in the examination procedure The first question is whether the field siz s used in 1975 were greater than those usual in 1960 This could be determined from a comparison of the measured change in energy imparted from 1960 to 1975 and the change that could be calculated from registered exposure data Such a comparison (based on relatively few recorded exposure data) indicates that most of the increase in energy imparted is explained by a change in exposure data

Thus th main reason for the enhancement in energy imparted per exposed film is an increase in the thickness of the irradiated volume There is a change in the examination technique which points to this Three to four of the films exposed in 1975 are zonographies while no zonographies were taken in 1960 A tilting of the patient during some exposures (giving about 30 per cent higher energy imparted) was more common in 1975 than in 1960

During part of the investigation the ureters are compressed The area of compression lies caudally to the examined volume and leads to an increase in the thickness of the patient in that volume About 30 mm increase in thickness requires a doubling of the energy imparted for a constant exit exposure (TROUT et coll 1952)

Finally a speculative explanation could be a general increase in the patient thickness OTTO (1976) investigated the average height and weight amongst Swedish 18 year old boys and recorded a 1 5 per cent increase in height from 1956 to 1971/72 and during the same period a 3 9 per cent increase in weight Such an increase corresponds to an increase of not more than 10 per cent in the energy imparted

The change in radiation quality since 1960 is an important reason for the non apparent decrease in dose It results in a manifest increase of the absorbed dose in superficially located organs such as the breasts and could only be motivated by an improvement in the image quality According to LÖFVANDER THAPPER (1977) enhancement in radiographic contrast (with iodine containing contrast media) with reduced high tension is somewhat limited with large fields No grid was used in the latter investigation and according to HONDIUS BOLDINGH (1961) the contrast im

tually less compression of the patient. The risk for this is greatest with the use of automatic brightness stabilization and automatic exposure control, where in both cases the physician is not aware of the change in exposure data. The image quality may improve partially due to reduced scattered radiation on the screen. In any case the present results do not support the proposal by FRIK & SCHOTT (1970) and STIEVE (1970) that image intensifiers should have automatic brightness stabilization. Warnings concerning the exposure rate increase with small radiation fields (COLE 1972, HENSHAW 1977) and due to decentering of the sensitive area (SVAHN 1977 b) have also been raised.

An apparent tendency exists for increased patient irradiation from radiography with automatic exposure control for all types of examinations. Besides the possible explanation mentioned, it could also be due to overexposure of the film.

The higher grid ratios in use during 1975 also imply that an angulation error leads to additional attenuation: with an error of one degree the attenuation difference between ratio 12 and ratio 6.5 is 10 per cent.

The discrepancy between calculated and measured energy imparted could thus be explained by poorer examination practice in combination with technical modifications, some of which failed to bring about intended improvements.

Full size chest radiography. The calculated relative energy imparted and the influence of different factors in lung examination do not differ much from the conditions in the gastrointestinal tract examination (Table 6). The primary filtration of the beam was in general higher in 1975, grids with ratio 12 and higher lead content were introduced and high speed screens used. The expected decrease in energy imparted per film exposed since 1960 was thus 30 per cent in examinations performed with rapid films in 1960 as compared with the examinations carried out with the least sensitive screen film system in 1975 (a day light loading system). Comparing with the more useful standard film in 1960 the decrease could be as much as 80 per cent.

The difference between expected and measured energy imparted is not as high as in the examinations of the digestive tract, however, in two of the examination rooms the measured energy imparted is more than double the expected value (Table 9). These are the rooms where the exposure times are very short, i.e. approximately 4 ms in one unit. According to SVAHN (1977 a) the radiation spectrum is changed considerably with a reduced number of high energy photons during such short exposure times. Part of the discrepancy could be explained by this effect, since the examination in reality is performed with a lower mean energy than expected, leading to increased attenuation in the patient and in the grid. However, as far as actual radiation qualities are concerned, the difference will not be great.

The radiation field has increased slightly: the largest film size was now 35 cm × 43 cm compared with 35 cm × 35 cm in 1960.

The higher grid ratios used in 1975 increase the risk for additional absorption due to angulation errors.

bilization in fluoroscopy may easily lead to a higher radiation dose to the patient when used improperly

Some improvements in the technique offer possibilities for dose reduction The rare earth intensifying screens are well known The air gap technique (RAO et coll and TROUT et coll 1975) is another means for reducing the dose per exposed film without loss of image quality Moving slit radiography is reported by several authors SORENSON & NELSON (1976) state that the entrance exposure of the patient can be reduced by a factor of 4 (which means about a factor of 3 in the energy imparted) without loss of image contrast

Significance of the present results for the population irradiation The results of the present limited survey cannot be the basis for any estimation of the level of the population irradiation but they could be used to calculate trends in this irradiation during the 15 year period The contribution from the four types of examination to the total irradiation of the Swedish population from diagnostic radiology appears in Table I The change from 1960 to 1975 was calculated considering the general increase in frequency of examinations of about 60 per cent from 1960 to 1975 (National Board of Health and Welfare 1976) and the measured change in energy imparted per procedure

A 30 per cent increase from 1960 to 1975 was estimated for the energy imparted in the individual The change in mean bone marrow dose per examination can be assumed to follow the change in energy imparted (confirmed for urography cf Appendix) and a 20 per cent increase in the individual mean bone marrow dose was estimated for the same period

If the same relation is true for the mammary dose the latter is increased by approximately 20 per cent When the radiation quality has been changed such as in urography the extrapolation from the energy imparted to dose in superficial organs is irrelevant The phantom experiments described in the Appendix indicate that a 20 per cent increase in the energy imparted from urography will render an 80 per cent increase in the absorbed dose in the breasts Consequently the individual mammary dose may have increased by approximately 60 per cent

Since it is not clear how universal the change in energy imparted observed at the University Hospital in Lund is it cannot be stated with certainty that the calculated trend in population irradiation is valid for the whole of Sweden however nothing indicates that the estimate is unrealistic According to BENGTSSON et coll the overall increase in gonad dose for different examinations is about 90 per cent for females and 10 per cent for males

The individual energy imparted mean bone marrow dose and mammary dose from the examinations were also estimated according to the possible dose reduction calculated from technical modifications In general it was about a factor of 2 lower which is in agreement with BENGTSSON et coll who state that a dose reduction of that magnitude is possible in diagnostic radiology in Sweden

provement factor of the grid increases between 90 kV and 70 kV The optimum quotient between energy imparted and contrast is obtained at definitely higher potentials than in use today (DREXLER & GOSSRAU 1973 LÖFVANDER THAPPER)

The image quality achieved in 1960 and 1975 was compared by BOIJSEN (1977) in a limited number of urographies (about 10 from each period) He observed an improved quality in 1975 which was believed to be of diagnostic significance

Spine hip and pelvis As in urography the tube potential has been reduced since 1960 from 100 kV to 70–83 kV The additional filtration is almost the same The other technical factors have changed in the same manner as for the other types of examinations and a total decrease of 70 per cent in energy imparted is expected (Table 6) In practice this decrease is obtained in the examination room with automatic exposure control while the energy imparted per exposed film in the other examination room is somewhat higher than calculated (Table 6) Since the number of examinations especially in 1960 is relatively low the disparity between calculated and measured energy imparted is hardly significant

The difference between the two examination rooms in 1975 is however common to all types of skeletal radiographic procedures which indicates that automatic exposure control is advantageous for the patient irradiation in these procedures

Conclusion

This work involved an extensive effort to determine the influence of various technical modifications on the patient irradiation in diagnostic radiology An unexpected low decrease in the energy imparted was revealed by the comparison between the 1960 and 1975 measurements A large part of the discrepancy between calculated and measured energy imparted may be explained by the factors discussed

The optimisation of any radiologic practice (including diagnostic radiology) as recommended by ICRP (1977) implies that the procedures should be subject to a cost/benefit analysis of technical improvements This work has demonstrated that it is also necessary to consider the corresponding technical changes when calculating the net benefit of a modification A change to more sensitive rare earth intensifying screens is shown by ELLIS and TAYLOR (1977) to be a relatively cheap measure for reducing irradiation of the population However the decrease in screen film exposure could be lost by other technical adjustments to improve the image quality but resulting in increased irradiation of the patient Suggestions of lowering of the high tension (STABLES et coll 1977) and augmenting the lead content of the grids (STRID) have been put forward

It is frequently emphasized that education is the most important factor for the reduction of the irradiation of the patient (ELLIS ICRP 1977) which is also supported by this investigation Some technical modifications such as brightness sta

Acknowledgements

This work is to a great extent a synthesis of several discussions with staff members in radiology departments and with manufacturers of radiologic equipment. Some of these discussions are referred to in the References as personal communications. I wish to express my sincere gratitude to Prof. Carl Carlsson and Prof. Kurt Lidén for their encouragement and valuable suggestions and to the radiographers for help with the measurements. This investigation was supported by grants from the Swedish Cancer Society.

SUMMARY

A comparison of the energy imparted during diagnostic radiographic procedures at the University Hospital in Lund during 1958 to 1960 and during 1974 to 1976 revealed an unexpected low decrease during the intermediate period. The influence of various technical factors on the irradiation of the patient was estimated and attempts made to explain the discrepancy between expected and measured energy imparted during 1974 to 1976. Considering the growth in frequency of examinations from 1960 to 1975 an increase in the population irradiation from diagnostic radiology is deduced for that period. The consequences of an optimum use of the technical modifications could have led to a decrease.

ZUSAMMENFASSUNG

Ein Vergleich zwischen der verabfolgten Energie im Zusammenhang mit Röntgenuntersuchungen an der Universitätsklinik Lund während 1958 bis 1960 und während 1974 bis 1976 ergab ein unerwartet niedriges Absinken während der zwischenliegenden Periode. Der Einfluss auf die Bestrahlung des Patienten durch verschiedene technische Faktoren wurde festgestellt und Versuche gemacht die Diskrepanz zwischen erwarteter und gemessener Energieergabe während 1974 bis 1976 zu erklären. Unter Hinsichtnahme auf den Zuwachs in der Frequenz von Untersuchungen von 1960 bis 1975 kann ein Anstieg der Populationsbestrahlung durch diagnostische Röntgenuntersuchung für diese Periode hergeleitet werden. Die Konsequenzen einer optimalen Anwendung von technischen Veränderungen hätten zu einem Absinken führen können.

RESUME

La comparaison de l'énergie transférée au cours d'examen de diagnostic radiographique à l'Hôpital Universitaire de Lund de 1958 à 1960 et de 1974 à 1976 a montré une faible diminution inattendue au cours de la période intermédiaire. L'influence de divers facteurs techniques sur l'irradiation du patient a été estimée et l'auteur s'efforce d'expliquer la discordance entre la quantité d'énergie transférée prévue et mesurée au cours de la période 1974–1976. En tenant compte de l'augmentation de la fréquence d'examens de 1960 à 1975 l'auteur déduit qu'il y a eu une augmentation de l'irradiation de la population par le radiodiagnostic. Un meilleur usage des modifications techniques aurait pu conduire à une diminution.

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Appendix

Phantom experiments The best phantom material for the present radiation energies was chosen from two available anthropomorphic phantoms the Rando phantom (ALDERSON et coll 1962) and a MIX D phantom (JONES & RAINE 1949)

Several authors have reported dose measurements on the Rando phantom in diagnostic radiology In the manufacturer s specification however no information on the tissue equivalency at such low energies is given On request the Alderson Research Laboratories specified the composition of the phantom material carbon 66 76 per cent by weight hydrogen 8 86 oxygen 21 11 nitrogen 3 10 and antimony 0 16 per cent by weight (STENSENG 19 6) The mass attenuation coefficient (m^2kg^{-1}) was derived by the conventional mixture rule using data from STORM & ISRAEL (1970) A comparison with the mass attenuation coefficients for water and muscle according to ICRU (1970) showed a good agreement down to 30 49 keV the K absorption edge of antimony At lower energies the Rando material has a considerably lower mass attenuation coefficient than muscle the ratio between the coefficients is 0 82 at 30 keV and 0 7 at 20 keV

The attenuation of the Rando material and water was compared by measuring the transmittance of monoenergetic γ rays in samples of equal size The calculated difference c ll not be confirmed with tellurium characteristic radiation from ^{125}I (AHLGREN 1976) However it was decided to use the MIX D phantom which according to calculations by HEMMINGSON & JUNG (1973) has a linear attenuation coefficient less than 15 per cent below that of water down to 10 keV

Only one phantom experimental series was performed the purpose was to determine the difference in organ doses due to the change in radiation quality in urography from 1960 to 1975 and to relate that difference to the disparity in energy imparted

The absorbed dose measurements were performed by thermoluminescent lithium fluoride ribbons (3 2 mm 3 2 mm 0 9 mm manufactured by Harshaw Chemical Co) read out on a Teledyne reader (Model 7300) The radiation qualities used were 84 kV with a total filtration of 4 mm Al (equivalent to the 1960 radiation quality) and 68 kV with a total filtration of 2 mm Al (equivalent to the lowest radiation quality used in 1975) At these energies the energy dependence of the dosemeters can be neglected Only relative measurements were carried out two dosemeters were placed at each measuring point and the total error of the measurements should be within 5 per cent The energy imparted was estimated from simultaneous measurements of the areal exposure

In urography the organs of main interest for potential radiation risks are breasts bon marrow ovaries and testes Dosemeters were accordingly placed on the phantom surfa at the approximate position of the breasts the testes and in a lattice over the irradiated area Dosemeters were also placed at the most frequent position of the ovaries according to NIK (1966) The mean bone marrow dose was derived from the surface exposure measurement according to ELLIS et coll (1975)

The results obtained were as follows for a given energy imparted by the two radiatio qualities the absorbed dose in the breasts was approximately 50 per cent higher at the lo e tension and filtration the testes dose (without gonad shield) about 20 per cent higher whil the ovary dose and the mean bone marrow dose was about the same To obtain the same ne density of the film about 50 per cent higher energy imparted was needed for the lower tub potential This implies the same increase in bone marrow and ovary dose while the mam mary dose is more than doubled (which is in agreement with the results of CARLSSO 1962)

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DIAGNOSTICALLY ACCEPTABLE LEVEL OF SECONDARY RADIATION

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Secondary radiation is generally considered to be harmful to image quality Whether this is a matter of the relative magnitude of secondary exposure is not fully known Thus a small proportion of secondary radiation reaching the recording medium has been regarded as favourable (Reiss 1963) in order to overcome the exposure threshold and to lower the effective contrast gradient thereby increasing the rather restricted exposure latitude of film screen combinations (cf Morgan 1946)

The harmful effect of secondary radiation has been assumed to be directly related to decrease in contrast (Wilsey 1921) In a previous report (Selin et coll 1976) evidence was produced indicating that the influence of secondary radiation is not a matter of simple reduction of contrast If the recording of the radiation relief had been a continuous process i e if the local density of the recorded image had been strictly determined by the local exposure rate in the relief this view would have been justified However the recording of roentgen quanta is a discrete process in which numerous quanta compete for a limited amount of receptor elements (grains) in the recording device If the total number of grains is low in relation to what is needed for a normally blackened image the element of competition between different quanta is increased This means that the impairment of image quality resulting from a given fraction of secondary radiation is higher than it would have been if the total number of grains had been large Thus in a perfect recording system providing an endless reserve capacity of grains the influence of secondary radiation may be expected to be

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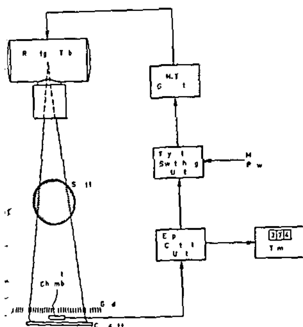


Fig 1 Experimental set up for radiography of high-contrast object

(Minnesota Mining & Manufacturing Co) The films were processed in an automatic developing machine (Pakorol) using a 2 5 min process at 25 5 C (developer G 138 Agfa Gevaert) The images were contact printed on film (Gevatone N 33 p Agfa Gevaert) which was also developed by the automatic process The grain of the Gevatone film being considerably finer than the granularity of the original films the prints could be enlarged without introduction of interfering graininess Moreover due to the modulation transfer high frequency cut off the printing reduced the graininess of the radiographic images implying low pass spatial filtration (SELIN & REICHMANN unpublished observation) The prints were examined by a photographic microscope micrograms (×10 ×25) being produced on film (Agfapan 25 Agfa Gevaert) by means of automatic exposure control

With the water scatterer placed close to the tube images were produced with virtually no secondary radiation in the image field the exposure time then being t_0 Several exposures were then made with the scatterer approaching the grid the amount of secondary radiation thus increasing and the exposure time now being t Assuming the exposure rate due to primary and secondary radiation in the recording plane to be $\dot{X}_p$ and $\dot{X}$ respectively the equation

$$\dot{X}_p t_0 = (\dot{X}_p + \dot{X}\ ) t \tag{1}$$

is applicable and the relative amount of secondary radiation obtained as

(2)

simply one of decreased contrast which may be fully compensated for by means of high contrast copying. However this is practically never the case (REICHMANN, unpublished observations). With increased secondary exposure many image details tend to disappear from the image and they cannot be made to reappear by any type of high contrast copying; they have simply been lost. Thus roentgen films are far from perfect recording devices in this sense. This leads to the conclusion that calculations are not useful in estimating how large a fraction of secondary radiation may be considered acceptable in diagnostic radiology.

Secondary screening can be improved considerably although at the expense of increased loss of primary (image forming) radiation (cf. STRID 1976). Thus improved secondary screening entails increased patient dose and tube load for the same number of primary quanta to reach the recording device. If the total number of quanta giving rise to blackening of the image is to be kept constant, the patient dose and tube load will be even higher when secondary screening is improved. However recent developments of intensifying screens indicate that the exposure may be kept constant if screens of increased speed are used. Thus the sensitivity of a rare-earth screen may be ten or more times as high as that of standard calcium tungstate screens without significant loss of high frequency response; a rare earth screen may be twice as sensitive as the tungstate screen (ROSSI et coll. 1976). Two general cases may be considered. One implies that the additional attenuation due to improved screening is counterbalanced by the use of rare earth screens of slightly higher speed than traditional screens, yet yielding unchanged image quality. The second case implies that considerably more efficient screening is introduced and high speed screens of lower image quality than was used earlier are employed in order to keep patient exposure constant. In the first case improved image quality may be expected. The second case however has not been tested. The aim of the present investigation is to illustrate that improved secondary screening may be recommendable even in the second case when screens of very high speed have to be used despite their impaired high frequency response and more unfavourable noise characteristics.

Recording of a high contrast object

Experimental. A scattered ray grid (linear strip density 40 cm^{-1}, grid ratio 10) was exposed in a stand for chest radiography (type MAS, Siemens Elema) with 1.50 m focus–film distance (Fig. 1). Secondary radiation was produced by a water scatterer of 0.25 m thickness placed in the radiation field at a variable distance from the grid. The exposure of radiation reaching the recording cassette was determined by the automatic exposure control system, a dominant ionisation chamber being inserted between the grid and the cassette and a digital electronic timer with 0.01 s resolution being used to determine the exposure time.

Two recording systems were used: X-Omatic Regular screens (Eastman Kodak Co) with Red Seal film (Ilford Ltd) and Trimax Alpha 4 screens with Trimax XD film

Table

Intensifying screens and exposure data used in radiography of low-contrast object

Screen	Relative exposure required	Relative exposure applied: primary X_p	Relative exposure applied: secondary X_s	Relative amount of secondary radiation X_s/X_p
X-Omatic Regular (Eastman Kodak)	10	10	0	0
		8	2	0 25
		7	3	0 43
		6	4	0 67
		4	6	1 0
		3	7	2 33
		2	8	4 0
Special (Siemens)	7	7	0	0
		5	2	0 40
		4	3	0 75
		3	4	1 33
		2	5	2 5
Azuray II (Philips)	4	4	0	0
		3	1	0 33
		1	3	3 0
MR 400 (Agfa-Gevaert)	4	4	0	0
		3	1	0 33
		1	3	3 0
Titan (Siemens)	3	3	0	0

xposure and varying secondary radiation exposure that the image quality deteriorates apidly with the amount of secondary radiation Not only does the image contrast ecreas but image detail is irreversibly lost as well The images look fragmented Fig 3) even though all image details were produced from a radiation relief having he same information content (the same number of image forming quanta)

It was seen moreover that the amount of secondary radiation is of decisive im portance to image quality Thus the faster screens in spite of their inevitably increased quantum mottle at lower exposure render the image with rather high fidelity as long as the secondary exposure is kept low whereas the slower fine textured screens do not reproduce fine details even for $\nu = 0.67$ i e with the secondary exposure equalling 40 per cent of the total exposure

Discussion

It is immediately clear from these experiments that secondary radiation should be reduced to the lowest level possible Even a small amount of non informative

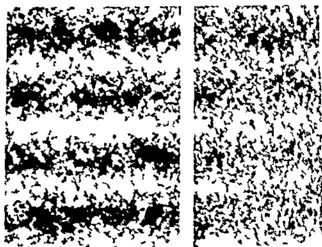


Fig. 2. Scattered ray grid (strip density 40 cm^{-1}, ratio 10) exposed with Trimax Alpha 4 screens and Trimax XD film (a) in the absence of secondary radiation and (b) with 40 per cent secondary radiation (ψ = 0.65) (× 50). Besides impaired contrast, the secondary exposure has caused loss of definition. The contrast differences between the images have been greatly reduced in printing. Still an obvious difference in information content remains.

The present experiment was performed in the range $0 \leq \psi \leq 0.7$, i.e. with the exposure due to secondary radiation amounting to 40 per cent or less of the total exposure in the recording plane.

Result. A relatively moderate amount of secondary radiation is detrimental to imaging (Fig. 2). For as low a ψ value as 0.3, i.e. the secondary exposure being ≈ 23 per cent of the total exposure, a fragmentation of the image occurs which cannot be reversed by post exposure image processing.

Recording of a low-contrast object

Experimental. A wax cast of the vascular tree of a human kidney was used as an object to obtain a radiation relief rich in weak signals of varying spatial frequency. Images were produced at 60 kV and 0.8 mm Cu filter at 1.0 m focus–film distance, on Curix RP 1 film (Agfa Gevaert) in aluminium cassettes with various screens (Table).

The high tension generator was set to deliver 1/10 of the exposure needed for yielding density 1.2 with the X Omatic Regular screens and the total exposure was obtained by exposing as many times as was necessary to achieve density 1.2±0.1 with the screens actually used. Part of the total exposure was given with no object present in the field, thus simulating secondary (non informative) radiation.

After machine processing, the films were inspected ocularly. Detail rich areas were contact printed on Gevatone N 33 p and subsequently enlarged (×3.5) on high contrast film.

Result. By the enlarged prints, all the relevant information of the original images was displayed and the rendering of details of varying size and contrast was readily demonstrated.

It was observed generally for images produced with the same primary radiation

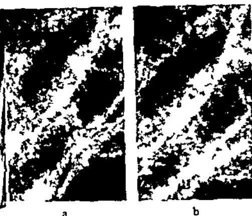
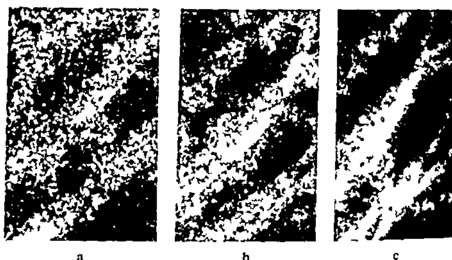


Fig 4 Same object as in Fig 3 exposed with (a) Kodak X Omatic Regular screens primary exposure 7 units secondary exposure 3 units (b) Siemens Titan screens primary exposure 3 units no secondary exposure The information content is about the same Since the Titan image (b) was obtained at 3/10 of the exposure used with Regular screens (a) Titan screens allow improved secondary screening even at the expense of a considerably increased loss of primary radiation

owing to removal of the small fraction of non informative radiation The Titan image was actually easier to inspect due to better contrast The improved secondary screening could in this case be instituted at the expense of a reduction of primary radiation by 4/7 In clinical practice any screening device stealing less than 4/7 of the primary radiation would give rise to improved imag quality despite the use of screens of much higher speed

In many diagnostic procedures of today an exposure of 30 per cent of secondary adiation represents a state of very efficient secondary screening (STRID 1976) Actually the present experiments have demonstrated that a grid designed for chest radiography transmitted so much secondary radiation from a 25 cm water phantom 90 kV radiation view field size 18 cm × 24 cm) that 40 per cent of the total exposure to the film consisted of non informative quanta ($\psi = 0$ 64) The grid technology of today represents a compromise Designers have avoided aiming at highly efficient grids since during the time when all recordings were made by means of calcium tungstate screens it was generally thought that a very efficient grid would cause too much loss of speed Today when high speed recording devices are available (new screen types intensifier fluorography etc) the whole matter of secondary screening must be seen in a new light In the earlier days when the grids now in use were designed films contained more silver and were probably not adversely affected to the same degree by a given fraction of secondary radiation as are modern films Rising costs for film manufacture will probably lead to a further lowering of the silver content of the films This in turn makes it mandatory that none of the grains available be wasted on recording of non informative quanta

The image of the radiation relief reaching the recording device is mainly dependent on three factors viz. the spectral distribution of the radiation the focus dimensions of the tube and the *selectivity of the* secondary screening device If the two latter factors are considered a striking imbalance is evident insofar as enormous sums have been spent on the design of new tubes yielding focus dimension improvements



a b c

Fig 3 Kidney vessel cast exposed with constant primary radiation (X_p) using (a) Kodak X Omatic Regular screens secondary exposure 1 5 Y_p (b) Siemens Special screens secondary exposure 0 75 Y_p (c) Agfa Gevaert MR 400 screens no secondary exposure enlarged prints (3) Increased screen speed compensates for the removal of secondary exposure Contrast was equalised in printing Reduced secondary exposure entails increased information content despite impaired screen performance

radiation is more harmful than might be supposed from the mere reduction of contrast The secondary radiation reduces the number of silver halide grains in the film that are available for recording of the information proper Since the number of grains is already small (STEIN & REICHMANN 1977, REICHMANN et coll 1978) no further reduction can be accepted without adversely affecting image quality

In recent years (STEVELS 1975) screen–film combinations have been evaluated with regard to their quantum detection efficiency (QDE) This quantity describes in principle how large a fraction of the exposure reaching the recording device contributes to the final image (cf JONES 1963 DAINTY & SHAW 1974) A large QDE value indicates high image quality for a given value of the exposure However since the recording device is exposed to both primary and secondary quanta the detection efficiency of real importance for the whole radiographic system is that pertaining to primary quanta Thus the screen–film combination should be considered together with the secondary screening device in order to formulate detection efficiency for primary quanta in relation to exposure given to the patient The present experiments indicate that this type of evaluation might drastically change the radiographic routine techniques so that heavier grids are installed and used in conjunction with screen–film combinations of extreme speed a highly efficient secondary screening apparently being of greater importance for the final detection efficiency for primary quanta than the unsharpness and noise characteristics of the screens This is amply illustrated by Fig 4 The X Omatic Regular 7 3 recording (30 % secondary radiation $\psi = 0\ 43$) is compared with the Titan 3 0 image The speed of the screens is changed by a factor 3 3 Still the information content of the films is about the same

performances intrinseques des ecrans rapides Ainsi l utilisation d écrans rapides permet l améliorer l elimination du rayonnement secondaire meme si ceci se fait aux depens d une plus grande deperdition de rayonnem nt primaire aboutissant à des images radiographiques le meilleure qualite d ensemble

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of rather marginal importance while grids have remained unchanged for severl decades It is suggested that attempts be made to produce new radiographic tech niques where the proportion of secondary exposure is lowered A realistic figure to start with at present seems to be an upper limit of 25 per cent of secondary radiation ($\psi \lesssim$ 0 30)

SUMMARY

Radiography of a high contrast object with a varying proportion of secondary radiation exposure showed that secondary radiation besides impaired contrast causes loss of image definition If the secondary exposure amounts to 25 per cent of the total exposure frag mentation of the image occurs which cannot be reversed by subsequent image processing The over all performance of intensifying screens of varying speed and for a varying pro portion of secondary radiation was analysed from films of a kidney vessel wax cast Fast screens with reduced secondary exposure yielded a higher image information content than high definition screens in the presence of secondary radiation despite the impaired function of the fast screens proper Thus the use of fast screens allows secondary screening to be im proved even at the expense of increased loss of primary radiation yielding radiographic images of higher over all quality

ZUSAMMENFASSUNG

Die Rontgenuntersuchung eines Objekts von hohem Kontrast mit einem unterschied lichen Verhaltnis von Sekundarstrahlen Exponierung zeigte dass die Sekundarstrahlung neben einem verschlechterten Kontrast einen Verlust der Abbildungsdefinition verursacht Falls die Sekundarstrahlung 25 Prozent der gesamten Exponierung ausmacht tritt eine Fragmentation des Bildes auf die nicht ruckgangig gemacht werden kann durch eine nach folgende Bildbehandlung Die Gesamtfunktion von Verstarkerfolien mit verschiedener Geschwindigkeit wurde bei einem unterschiedlichen Anteil der Sekundarstrahlung an Filmen von Nierengefass Wachsabgussen analysiert Schnelle Folien mit verminderter Sekundar strahlung gaben eine hohere Bildinformation als Verstarkerfolien mit guter Definition in der Gegenwart von Sekundarstrahlung trotz der schlechteren Funktion der Folien Somit er laubt der Gebrauch von schnellen Folien eine verbesserte Sekundarabschirmung auch auf Kosten des grosseren Verlusts der Primarstrahlung wodurch eine verbesserte Gesamtquali tat der Rontgenbilder erreicht wird

RÉSUMÉ

La radiographie d un objet de contraste élévé réalisée avec une proportion variable d exposition au rayonnement secondaire a montré que le rayonnement secondaire non seule ment diminue le contraste mais cause aussi une détérioration de la définition de l image Si l exposition au rayonnement secondaire atteint 25 pour cent de l exposition totale il se produit une fragmentation de l image qui ne peut etre corrigée par un traitement ultérieur de l image Les performances d ensemble d écrans renforçateurs de différentes vitesses et pour des proportions variables de rayonnements secondaires ont été analysées à partir de film d un moule en cire des vaisseaux rénaux Les écrans rapides avec une exposition réduite au rayonnement secondaire ont donné un meilleur contenu d information de l image que les écrans à haute définition en présence de rayonnement secondaire malgré les moins bonnes

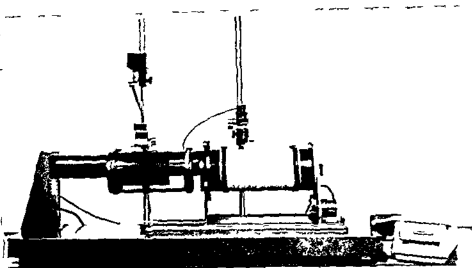


Fig 1 Photograph of apparatus The original film forms the cylinder to the left and the recording film the cylinder to the right Above each cylinder are light-emitting diodes and projecting lenses to the left an array of 10 10 red diodes and to the right a single green diode Light transmitted through the original film is reflected by a mirror onto a photomultiplier tube The mirror and photomultiplier tube are inside the left cylinder To the right is the punched-card reader

the digitilization storage and manipulation of the images imply large and costly computer systems (HARLOW et coll 1976) The prototype of a simple inexpensive device is now presented It combines a digital filtering technique with a reasonable speed and gives full size hard copies of the processed films

Material and Methods

General description The processing is performed with two-dimensional filtering in the image domain The photographic density in the original film is sampled in sequential overlapping square sub-images each containing 10 × 10 pixels The analog signals from the 10 × 10 pixels are individually multiplied by corresponding elements of a digital 10 × 10 filter matrix The elements of the product 10 × 10 matrix are electronically added analogously and the sum determines the amount of light directed onto a photographic emulsion The films carrying the original and final images are moved synchronously so that each sub-image in the former corresponds to one point in the latter

The original roentgenogram (24 cm × 30 cm) and the unexposed film are clamped to right cylinders of equal radius on a common central axis (Figs 1 2) The two films are rotated synchronously by a stepper motor The film motor assembly forms a sledge driven by another stepper motor via a thread axis On the sledge support are fastened a 10 × 10 array of red light-emitting diodes (physical diameter of each diode

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IMAGE ENHANCEMENT BY DIGITAL-ANALOG FILTRATION

I Technical description of device

J CEDERLUND A HEMMINGSSON B JUNG H LUNDQVIST and H O MOBERG

The rich abundance of detail presented in conventional roentgenograms makes the chance of certain perception of significant lesions low in some situations for example in the recognition of bone and pulmonary metastases (HEMMINGSSON et coll 1972 1975 HEMMINGSSON & LÖFROTH 1976) In the former case perception of the lesion is rendered difficult by superimposition of bone trabeculae and in the latter case the image of the lung is rich in detail Common to both situations is that the structure of interest has a rather low photographic contrast is relatively large and is located in an image containing numerous small structures of comparably high contrast

The aim of image filtration in these situations is therefore to reduce the effect of the distracting small structures and to improve the perceptibility of the details of interest

Image filtration can be achieved analogously by electronic filters in video chains (KUNDEL et coll 1969, FUCHS et coll 1972) or by optic techniques (GOODENOUGH et coll 1974) However it is difficult to obtain good filtering properties in two dimensions with such systems Digital techniques are superior in this respect but

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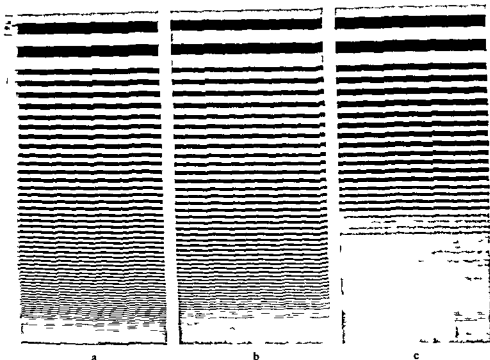


Fig 4 Films of a resolution test object a) Original film b) Processed with one light-emitting diode. Parameters set to high resolution c) Processed with low pass filter with some edge enhancement

Results and Discussion

The number of variables in the filtering process is large and it has not been possible to test all combinations

The light output from the diodes in the 10×10 array varied by less than $\pm 30\%$ from the mean A correction for this variation was applied in the elements of the filter matrices The optical projection of the 10×10 array could be varied between 2 mm × 2 mm and 20 mm × 20 mm The image could be blurred so that each diode sampled a suitable area of the sub image A large projected diode array on the original gave a processed image with little detail

The contrast of the processed image could be enhanced by an increase in the high tension of the photomultiplier tube and by increasing the numerical values of the filter elements The photographic density of the processed film could be varied by changes in the speed of the scanning process and in the setting of the bias potentiometer

The following is an extract from the results of the running in period The copying function of the apparatus was tested with an original film of a resolution test object and a film of a bone specimen All filtering elements in the filtering matrix were

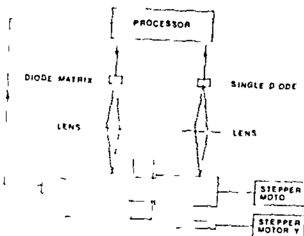


Fig 2 Principle of the device

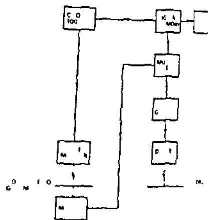


Fig 3 Block diagram of the electro construction

2 mm) and an optical system that focusses the diode light onto the original film. Vertically below the array and lens system and inside the cylinder formed by the original film is a mirror that reflects the transmitted diode light on a red sensitive photomultiplier tube placed horizontally and coaxially with the film cylinders. Above the unexposed film and rigidly coupled to the sledge support is a single green light emitting diode and a lens that projects the diode light onto the photographic emulsion of the recording film

Electronic construction A block diagram of the construction is given in Fig 3 An internal clock (100 kHz) pulses the diodes in the 10 × 10 array in sequence diode by diode and line by line The same clock also scans a digital memory (10 × 10 words of 12 bits) which is loaded from a punched card reader Each diode is lit for 3 μs and the pulse from the photomultiplier tube is amplified and multiplied by a 10 bit multiplier word from the memory in an analog to digital multiplier The multiplied pulses are summed with individually preselected signs determined by bit 11 of the multiplier word The sum of all 100 pulses from one complete diode array sweep determines the period during which the single green diode exposes the recording film is lit When the summed signal is zero the diode is lit for a certain fraction of the total sweep period This fraction is preselected with a bias potentiometer A positive summed signal adds to the period of lighting and a negative signal detracts from it The elements of the filter matrix can take values between −999 and +999 which provides for suitable accuracy both of the filters and of corrections of individual variations in the light output from the red diodes Correction factors are obtained from measurements of the photomultiplier tube pulses with a multichannel pulse height analyser and a uniform absorber between the diode array and the photomultiplier tube

Microdensitometry of the original and the filtered films was made with the microdensitometer Mark III CS (Joyce Loebl)

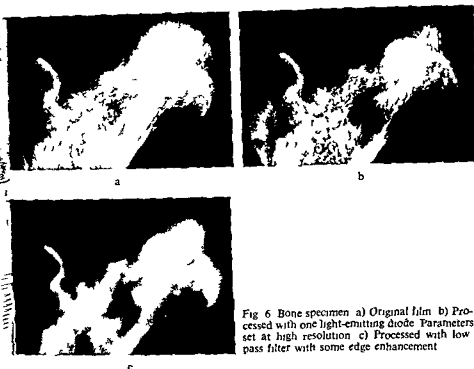


Fig 6 Bone specimen a) Original film b) Processed with one light-emitting diode Parameters set at high resolution c) Processed with low pass filter with some edge enhancement

original The effect of various filters on various test objects will be further discussed in forthcoming reports

In conclusion it was found that the apparatus fulfils the design criteria having an ability to filter image matrices containing more than 10^6 pixels with general 10 10 filter matrices It should be suitable for further analysis of filtration techniques

SUMMARY

A device for general (10 10 pixels) image filtration of 24 cm 30 cm roentgenograms in the image domain (10 pixels) is described It combines analog and digital techniques and records the processed image on film in the same scale as the original Results from preliminary tests of the equipment are reported and it is concluded that it yields images with increased perceptibility of large scale objects of low photographic contrast in the presence of disturbing structures of high spatial frequency and comparably high photographic contrast

ZUSAMMENFASSUNG

Eine Anordnung fur eine generelle (10 10 Pixel) Bildfilterung von 24 cm 30 cm Rontgen bildern im Abbildungsgebiet 10 Pixel wird beschrieben Dieses vereint analoge und digitale Verfahren und gibt die erhaltene Abbildung auf einem Film in der gleichen Skala wie

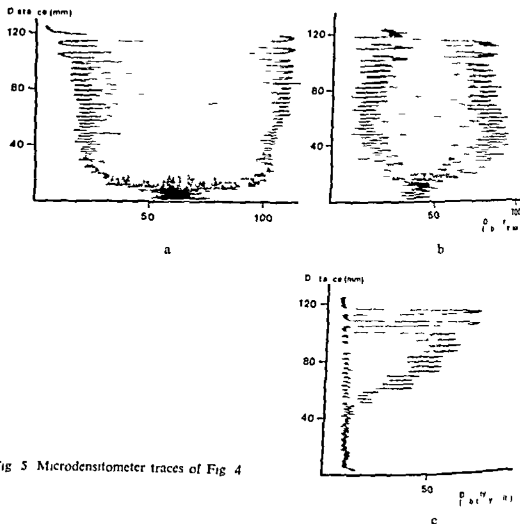


Fig 5 Microdensitometer traces of Fig 4

set equal to 0 except one central element The size of the projected image of the 10 × 10 array was 2 mm on the original and that of the image of the green diode on the recording film less than one mm in diameter The recording film was Trimax XM (3M) The drum rotated at 3 revolutions per second and the sledge movement was 3 mm/s The originals and the results of the copying procedure appear in Figs 4 and 6 It is evident from the films of the resolution test object and from microdensitometric measurements (Fig 5) that the apparatus copied structures down to 20 line pairs per cm The bone specimen was also copied with good accuracy down to fairly small structures (Fig 6 b)

Figs 4 c and 6 c give the results when a 10 × 10 filter matrix with some edge-enhancing effect was used The effect of this filter was to exclude spatial frequencies above 5 line pairs per cm (Figs 4 c 5 c) The filtered image of the bone specimen also lacks finer details (Fig 6 c) The more extended structures with rather small photographic density differences such as the bore hole and the sclerotic lesion in the lower part of the film are however better visible in the filtered image than in the

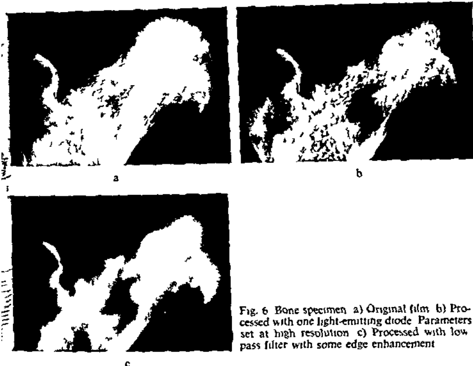


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derjenigen des Originals wieder Von vorlaufigen Prüfungen dieser Anordnung k geschlossen werden dass diese Anordnung Bilder mit niedrigem Wahrnehmbarkeit b grossraumigen Objekten mit niedrigem photographischen Kontrast in der Gegenwart von storenden Strukturen mit hoher raumlicher Frequenz und relativ hohem photographischen Kontrast herstellt

RÉSUMÉ

Les auteurs décrivent un dispositif pour la filtration générale d image (10 10 pixels) d radiographies 24 cm 30 cm dans le domaine d image (10⁶ pixels) Il combine les techniques analogique et digitale et reproduit l image traitée sur un film a la meme échelle que l original Les résultats d essais préliminaires de cet appareil sont présentés Les auteurs concluent qu il fournit des images ayant une perceptibilité accrue des objets de grande dimension et de faible contraste photographique en présence de structures genantes de grande fréquence spatiale et ayant un contraste photographique relativement élevé

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INFANTILE HEPATIC HAEMANGIOENDOTHELIOMA

Angiographic considerations

W MORTENSSON and H PETTERSSON

Infantile hepatic haemangioendothelioma may be solitary or multicentric being associated with extra hepatic haemangiomas in about one third of the cases pre dominantly in the skin The lesion has a microscopically benign appearance and may be asymptomatic and detected incidently Nevertheless it is potentially lethal death being caused by intractable heart failure or haemorrhage (MCLEAN et coll 1972)

The triad of hepatomegaly congestive heart failure and cutaneous haemangiomas strongly suggests the diagnosis usually the definitive diagnosis is made at microscopy of a biopsy specimen During the past decade several reports on angiography of the lesion have appeared (Table) Based on these reports and on 3 cases observed at this department the specificity of the angiographic findings is now discussed

Case reports

Case 1 Girl (previously reported by KORNFALT et coll 1975) At 5 weeks of age an en larged liver was detected as well as several small cutaneous haemangiomas Liver scinti graphy ($^{99}Tc^{m}$ sulphur colloid) demonstrated multiple defects in the enlarged liver At laparotomy 3 weeks later *multiple* tumours of varying sizes were observed in the liver Microscopy of a surgical biopsy specimen revealed haemangioendothelioma with varying microscopic appearances Some central areas consisted of large irregularly dilated vascular

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Table

Reports on angiography of infantile hepatic haemangioma

References	Age of patient	Type of angiography
DeLorimier et coll (1967)	2 weeks	Aortography
Pantoja (1968)	5 months	Venous arteriography
Berdon & Baker (1969)	Newborn	Aortography
Slear & Cornell (1969)	2 weeks	Aortography
Rake et coll (1970)	1 month	Aortography
Moss et coll (1971)	2 days	Aortography
	7 weeks	Aorto-coeliacography
Tawes et coll (1971)	2 days	Aortography
Leonidas et coll (1973)	2 months	Aortography
	1 week	Aortography
Globl & Kauffman (1974)	2 months	Aortography
Slovis et coll (1975)	1 day	Aortography
	1 day	Aortography
Jackson et coll (1977)	6 months	Coeliacography
Stanley et coll (1977)	Newborn	Aortography
	2 days	Aortography
	7 months	Aortography
Tegtmeyer et coll (1977)	3 weeks	Coeliacography
Present authors	2 months	Aortography
	2 months	Aorto-coeliacography
	2 weeks	Aorto-coeliacography

spaces lined by a single row of elongated endothelial cells but most parts contained numerous small vessels with proliferating plump lining cells in several layers No evidence of malignancy

One week after operation the girl developed congestive heart failure The heart volume increased and the pulmonary vessels became wide Catheterization of the heart and cardioangiography were performed to exclude congenital heart malformation Angiography of the liver was made on the same occasion

Anticongestive therapy had no satisfactory effect on the heart decompensation Therefore radiation therapy was instituted (^{60}Co ventral field covering the liver 10 Gy given during one week) The heart insufficiency gradually diminished during the treatment the total blood volume became normalized and the liver function tests remained normal At repeat liver scintigraphy the multifocal tumours had disappeared and the liver had decreased in size

At repeat examinations 3 and 3½ years after the first admission the girl was healthy and physical examination revealed no abnormalities

Case 2 Girl The mother of the patient had rubeola during the first trimester During the first days of life the girl had episodes of cyanosis She had no obvious signs of cardiac insufficiency but the heart volume increased and the pulmonary vessels were wide All symptoms and signs disappeared spontaneously in 2 or 3 days At the age of 5 weeks an enlarged liver was detected incidentally No skin abnormalities were observed Liver scintigraphy demonstrated one large central defect and possibly some small peripheral defects in the uptake A few days later laparotomy was performed during which a liver biopsy was to be



Fig 1 Case 2 The aorta decreases abruptly in width below the wide coeliac artery

taken However the puncture of the liver caused profuse bleeding which was difficult to stop No biopsy specimen could be obtained Coeliac angiography was performed at the age of 7 weeks

Transient dyspnoea and cough appeared during the week following the operation The girl improved spontaneously and she was discharged a few days later in good condition The total blood volume which was increased during the first month of life gradually became normal Repeat scintigraphy demonstrated that the liver size had become normal and that the tumours had disappeared Liver function tests remained normal Now more than 4 years later the girl is healthy and her physical and mental development is normal

Case 3 Boy Immediately after birth an enlarged liver was palpated No skin abnormalities Liver scintigraphy demonstrated an enlarged liver without evident defects but the right lobe was displaced by an extrahepatic tumour The boy had no signs of cardiac disease The heart volume and pulmonary vessels were normal Coeliac angiography was performed No therapy was given

The boy who is now 2 years old has been regularly re-examined His development is normal The liver has gradually decreased in size Liver function tests have remained normal

Angiography

Aortography at 2 months of age was performed in Case 1 via injection into the left ventricle of the heart In Cases 2 and 3 abdominal aortography and selective

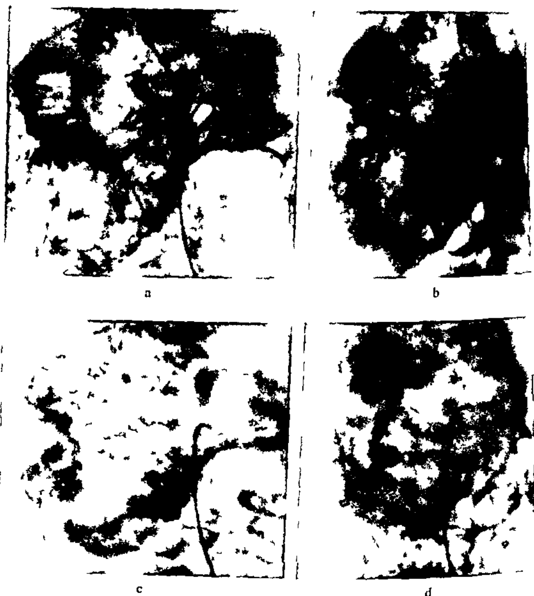
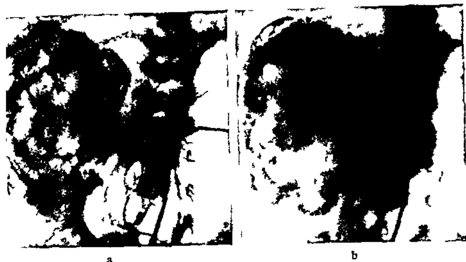


Fig 2 Case 2 Coeliac angiography Large vascular tumour involving the right and intermediate hepatic lobes The arterial branches wide stretched and non tapering Initially vascular tumours close to the large branches gradually tumours become visible also between the branches The tumours drain into large irregular veins The right hepatic lobe is surrounded by a haematoma 2 to 3 cm thick

angiography of the coeliac axis were performed at the ages of 7 and 3 weeks respectively

The abdominal aorta narrowed abruptly below the coeliac axis (Fig 1) The coeliac and hepatic arteries were wide

The liver was markedly enlarged and the vascular malformation involved the entire liver in Case 1 the right and intermediate lobes in Case 2 and the moderately enlarged right lobe in Case 3 The demarcation between affected and unaffected



ig 3 Case 3 Vascular tumours in the periphery of the right liver lobe surrounding large avascular reas

iver parenchyma was distinct (Figs 2 3) Case 2 had also a large perihepatic haema oma due to bleeding following needle puncture performed 10 days earlier (Fig 2 d)

In all 3 cases the intrahepatic arterial branches were wide and stretched and traversed the tumour without being displaced The branches did not taper towards the periphery (Figs 1-3) In the early arterial phase clusters of vessel rich lesions appeared along the arteries (Figs 1-3) Gradually a great number of other similar tumours became visible diffusely spread in the affected lobe (Fig 2 b) Contrast medium pooled in the tumours disappeared slowly Large and apparently completely avascular areas also existed most evident in Case 3 (Fig 3 b)

The hepatic veins were demonstrated in Case 1 only but large capsular or subcapsular veins were outlined in all 3 cases (Figs 2 3)

No shunting of contrast medium occurred between the hepatic arteries and intra hepatic branches of the portal vein After injection into the lumbar aorta the portal vein and its intrahepatic branches were demonstrated in Cases 2 and 3 although they were too faintly outlined to allow a close assessment

In no case were irregular vessel walls observed nor vessels with a zigzag course vascular encasement or interruption or other appearances suggesting malignancy

Discussion

Two main types of haemangiomas can be recognized in infants namely cavernous haemangiomas and haemangioendotheliomas (GRAIVIER et coll 1967 BAGGENSTOSS 1970) Classification of the hepatic vascular tumours has however been a subject of controversy variations in the microscopic appearances of the haemangioendo-

theliomas have contributed to the difficulty (McLEAN et coll) The unspecified term hepatic angioma is often used in the literature to circumvent the classification difficulties

Cavernous haemangiomas are much more rare in infancy and childhood than are haemangioendotheliomas (EDMONDSON 1956 ARIEL & PACK 1960, DEHNER & ISHAK 1971) However, in regressing haemangioendotheliomas foci of cavernous haemangioma may appear (DEHNER & ISHAK) The cavernous type of hepatic angiomas is usually asymptomatic and found incidentally at autopsy while haemangioendotheliomas have a tendency to cause heart failure and haemorrhages (EDMONDSON, ARIEL & PACK DEHNER & ISHAK)

The diagnosis was established at microscopy in 12 of the cases listed in the Table In the remaining patients the clinical course including spontaneous healing of the tumours, corroborated the impression of the benignity of the lesion

The angiographic appearance of the haemangioendotheliomas was identical in all the present cases and in 13 of those previously reported The salient angiographic features were wide intrahepatic arteries which were stretched but not displaced by the tumours and which did not taper towards the periphery clusters of abnormal vessels which were gradually filled with contrast medium and were first visible close to the large arterial branches and vascular areas without evidence of malignancy In 4 cases the quality of the films presented was unfortunately too poor to allow a close evaluation In a series of 14 cases of children with malignant hepatomas and 12 with hepatic neuroblastomas the findings differed from those described

Two cases of infantile hepatic cavernous haemangioma examined with angiography and considered to be confirmed at microscopy, have been reported (SLOVIS et coll 1975 STANLEY et coll 1977) Both instances concerned newborns with a large liver and heart decompensation In the first case the angiographic features were identical with those now summarized However the correctness of the microscopic diagnosis is not convincing the scanty information on the histologic features given in the primary report (BERDON & BAKER 1969) may rather agree with those of a haemangioendothelioma In the other case the angiographic abnormalities did not resemble those which in the present report are considered characteristic of haemangioendothelioma

The malignant variety of haemangioendothelioma is extremely rare and seems to affect mainly adults and to some degree also children but has not been observed in infants (KAUFFMAN & STOUT 1961 DEHNER & ISHAK) Only one case of malignant haemangioendothelioma examined with angiography is on record (FREDENS 1969) The findings seem to deviate clearly from those encountered in the benign form It is worth mentioning that a benign haemangioendothelioma at microscopy may easily be considered as a malignant form because of the increased number of mitoses usually present in the endothelial cells (EDMONDSON ARIEL & PACK)

Liver scintigraphy offers a well documented method for diagnosing hepatic mass lesions In 2 of the present cases scintigraphy proved useful in demonstrating an

larged liver and defects in the uptake due to absence of phagocytizing Kupffer lls within the tumours The results agreed with those of previous reports (SLOVIS coll STANLEY et coll)

STANLEY et coll emphasized the value of dynamic scintigraphy in diagnosing patic angiomas By repeat imaging of the emission during the first minutes after travenous administration of the isotope an arterial and a venous vascular phase uld be successively depicted and finally the amount of activity of the colloid tained in the liver be determined Vascular tumours exhibited high activity initially ue to the abundance of tumour vessels but low activity in the later stage due to the bsence of phagocytizing capacity The examination modality has however a low pecificity and cannot differentiate haemangioendothelioma from other richly vas ularized tumours supplied by the arterial system In the present case no dynamic intigraphy was used only static which was found valuable in monitoring the ealing process

The natural course of the cutaneous haemangiomas is characterized by progression luring the first 3 months of life followed by regression and the tumour may disappear ompletely during the first years of life (LAMPE & LATOURETTE 1959 MARGILETH & MUSELES 1965) Hepatic haemangiomas probably present a similar course Spon aneous complete regression of hepatic haemangiomas has been reported (PACKARD & PALMER 1955 EDMONDSON CROCKER & CLELAND 1957 McLEAN et coll) Thi course occurred in at least 2 of the present cases

The risk of developing heart failure depends on the amount of vessel rich tumour tissue providing for large arteriovenous shunts If heart failure has occurred the mortality rate in untreated cases may amount to 80 to 90 per cent (DELORIMIER et coll 1967 JACKSON et coll 1977) When intense anticongestive therapy fails to bring relief administration of corticosteroids (ROCCHINI et coll 1976) partial liver resection (BERDON & BAKER LEONIDAS et coll 1973 TAWES et coll 1971) ligation of the hepatic artery (DELORIMIER et coll RAKE et coll 1970 GLÖBL & KAUFFMAN 1974) or radiation therapy (RAKE et coll) have all been recommended The effect of irradiation and administration of corticosteroids is difficult to evaluate because of the strong tendency of the tumour to heal spontaneously Embolization with Gelfoam was used in one instance but resulted in fatal complications (TEGTMEYER et coll 1977) at autopsy particles of Gelfoam were found in the lungs and in interlobar renal arteries

Angiography gives the diagnosis and provides detailed information on the vascular morphology which may be pertinent on surgical intervention Assessment of the size of the tumour may give some hint of the risk that therapy resistant heart failure develops

Surgical biopsy has generally been used to establish the final diagnosis at microscopy However it involves the risk of inducing severe bleeding which may be difficult to manage Angiography appears to have such a high diagnostic accuracy that microscopy should not be considered an obligatory procedure

SUMMARY

Angiographic abnormalities in infantile hepatic haemangioendothelioma are analysed on the basis of previous reports and on 3 new cases It is emphasized that the high specif of angiography of the hepatic artery should make other diagnostic procedures unnecessary

ZUSAMMENFASSUNG

Angiographische Abnormitaten bei jugendlichen hepatischen Haemangio-endotheliomen werden analysiert auf der Basis von fruheren Beschreibungen und von 3 neuen Fallen Es wird hervorgehoben dass die hohe Spezifitat der Angiographie der Arteria hepatica andere diagnostische Verfahren unnotig machen sollte

RESUME

Les anomalies angiographiques de l hémangio-endothéliome hépatique infantile ont été étudiées sur la base des publications précédentes et sur 3 nouveaux cas Les auteurs soulignent que la haute spécificité de l angiographie de l artère hépatique devrait rendre inutile les autres méthodes de diagnostic

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FROM THE SECTION OF PEDIATRIC RADIOLOGY, DEPARTMENT OF DIAGNOSTIC RADIOLOGY
MALMÖ ALLMÄNNA SJUKHUS, S 214 01 MALMÖ, SWEDEN

OSSIFICATION OF FEMORAL HEAD IN INFANCY

I Normal standards

H PETTERSSON and G THEANDER

Current research in this department concerning deviations from the ordinary development of the hip has called for detailed standards for the normal ossifica[…] of the femoral head in the first year of life Normal standards have been publi[…] by various authors (ELGENMARK 1946 GARN et coll 1967 GROSSMANN 19[…] BERGMANN 1970 MOVSHOVICH & VILENSKY 1972 SCHMID 1973) but have […] proved informative enough for our purposes Available standards were consid[…] unsatisfactory also because they are either relatively old or have been obtai[…] from populations which might in some relevant respect differ from that of Swede[…] for example ossification may vary with ethnic and socio economic factors (ELGEN[…]MARK GARN et coll)

The present investigation was undertaken to establish standards for the norm[…] ossification in the population served by this department The application of th[…] standards is reported separately

Material and Methods

The material consisted of a p films of infants admitted to the department […] 1966 to 1976 they were obtained at examination of the abdomen or at urograp[…] in cases with no history of skeletal abnormality No films of prematurely bo[…] infants or infants with known or assumed chronic or recurrent disease were accepte[…]

Submitted for publication 2 March 1978

Table 1

Sex and age distribution of the 455 infants

	Age interval (months)												
	0–1	1–2	2–3	3–4	4–5	5–6	6–7	7–8	8–9	9–10	10–11	11–12	Total
of ls	40	19	16	13	16	15	21	10	16	14	16	18	214
of ys	44	43	22	26	17	18	11	12	11	12	10	15	241
al	84	62	38	39	33	33	32	22	27	26	26	33	455

The infants thus selected 455 in number (214 girls and 241 boys) had been ex amined because of a single episode of urinary infection or of abdominal symptoms or casionally because they had swallowed a foreign body They were grouped ac rding to age the width of the age intervals being 1 month The age distribution either sex is given in Table 1

In each age group of either sex the number of infants with visible ossification nters in the femoral heads was recorded as well as whether they were unilateral or ilateral The number of the femora with visible ossification center divided by the otal number of femora in the group is referred to in the following as the fraction of ssified heads

The shape of the ossification centers was also analysed and the size was measured on the films Since the examinations had not primarily been focused specifically on he hips the position of the legs had not been standardised hence the degree of otation of the femora was not uniform Such differences in position did not affect the evaluation of the ossification in the youngest age groups because the minute centers in this stage of development appeared spherical but on further growth the centers assumed a different shape The width of the centers as measured on the a p film may then differ considerably with the degree of rotation of the legs (Fig 1) On the other hand the height of the centers on the film proved largely inde pendent of such changes in position The evaluation of the size of the centers was therefore based on measurement of the height alone

Statistical analysis The fraction (f) of ossified heads at the age x was determined by a logistic function

$$f = \frac{1}{1 - e^{-\beta}} \qquad (1)$$

Using a computer the parameters α and β were estimated with the maximum like lihood method and the standard errors (SE) of the estimates were assessed according to large sample theory (Cox 1970) These calculations were based on the observed

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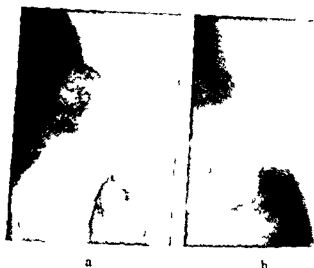


Fig 1 Girl aged 1 year a) a p and b) lateral view of right hip Height of ossification center equal but not dimensions perpendicular to height

number of femora with ossification centers in the various age groups using th midpoint of the age interval as characteristic age However, the number of infa —not the number of femora—was taken as sample size

Approximate 95 per cent confidence intervals of the log odds, $y = \alpha + \beta x$ w obtained as the estimated value of y plus and minus 2 SE of y These intervals w transformed into approximate 95 per cent confidence interval for f The log model was tested for lack of fit

The analysis of the height measurements was performed as follows All infa with no visible ossification of the femoral heads were excluded In infants with unilateral ossification the height of the absent center was given the value 0 In these cases and in those with bilateral ossification the mean height of both centers was treated as one observed value i e the number of means—not the number of measurements—was taken as sample size

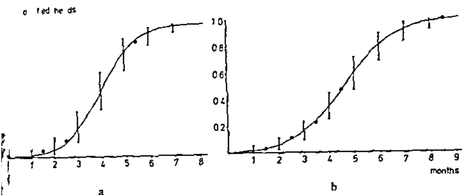
The mean height h was determined separately for either sex by linear regression on age x

$$h = a + bx \quad ([illegible])$$

Table 2

Number of infants with visible ossification center of femoral head in consecutive age groups Each infant with only unilateral center is indicated by a u

	Age interval (months)												
	0–1	1–2	2–3	3–4	4–5	5–6	6–7	7–8	8–9	9–10	10–11	11–12	Total
Girls	0	1	3uu	5	10u	13	21	10	16	14	16	18	1[illegible]7
Boys	0	2u	3u	6	9uu	14	9	11	11	12	10	15	10[illegible]
Total	0	3	6	11	19	27	30	21	27	26	26	33	[illegible]9



2. Fraction of ossified heads in the various age groups of either sex Dots observed values tical lines 95 confidence intervals Curves logistic functions a) Girls b) Boys

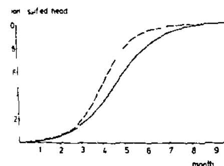


Fig 3 Diagram combining both curves in Fig 2 for comparison Girls — Boys

id the corresponding 95 per cent confidence intervals (prediction intervals) for the dividual mean heights at any age in infancy were calculated The fit of the regres on was tested with an F test (ARMITAGE 1971)

Results

The number of infants with visible ossification in the femoral head in the various ge groups is given separately for either sex in Table 2 It shows that such ossification lid not occur before one month of age but was invariably visible from 6 months of age in the girls and from 8 months in the boys The centers were bilateral except in girls and 4 boys These 7 infants are included in the numbers in Table 2 and ndicated by the letter u

The values obtained for the parameters α and β (eq 1) were

in the girls $\alpha = -5\ 51$ (SE 0 93)
$\beta = 1\ 38$ (SE 0 22)
in the boys $\alpha = -4\ 95$ (SE 0 65)
$\beta = 1\ 07$ (SE 0 15)

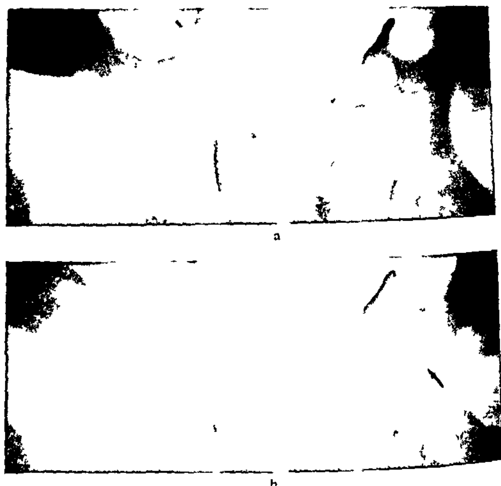


Fig 4 Girl a p views a) At 2 months 4 days Minute ossification center in right but not in left femoral head b) 13 days later Minute center in left femoral head (→) Increased size of right center

The tests for lack of fit of the logistic model showed no significance in any ca
Actually the fit proved exceedingly good for both sexes

The logistic functions representing the incidence of ossification of the femo
head according to age in either sex are graphically illustrated in Fig 2 which a
shows the 95 per cent confidence intervals Comparison of the two curves (Fig
reveals a somewhat later ossification in the boys than in the girls The median

Table 3

Mean height (in mm) of ossification centers in consecutive age groups

	Age interval (months)										
	1–2	2–3	3–4	4–5	5–6	6–7	7–8	8–9	9–10	10–11	1
Mean height											
Girls	2 8	1 9	3 9	4 2	5 0	5 9	6 7	7 6	8 1	8 4	9
Boys	1 5	2 1	3 4	3 5	4 3	5 2	6 1	6 7	7 6	8 3	

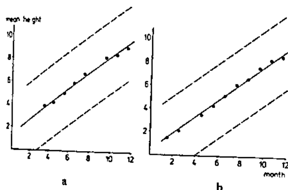


Fig 5 Height (mm) of ossification center according to age in infants of either sex Dots mean measurements Continuous lines regression lines Discontinuous lines 95 confidence limits (prediction intervals) for individual mean height a) Girls b) Boys

(which in a logistic function equals the mean age) at onset of the ossification was calculated to 4 0 months in the girls and 4 6 months in the boys This sex difference proved statistically significant (p<0 05)

The ossification of the femoral head was multicentric on one side in one boy and on both sides in 3 girls and one boy The age of these infants at the examination ranged from 2 to 6 months In all the other cases the femoral head had only one ossification center which appeared spherical as long as it did not exceed 2 mm in diameter On further growth the center became larger in maximum width than in height but its surface including the part towards the femoral shaft remained convex in all the age groups

In 5 of the 7 infants with unilateral ossification of the femoral head the center was only one mm in diameter suggesting that ossification had started shortly before the examination Repeat examination performed in one of these cases illustrated the rapid occurrence and growth of such small centers (Fig 4) In the remaining 2 infants the unilateral center was 3 mm in height Both of these infants were 4 months Repeat examination of one of them 14 months later demonstrated bilateral centers of equal size Unilateral ossification was not observed in any infant above 5 months

Of the infants with bilateral ossification of the femoral head both centers were practically equal in height in 186 girls and 195 boys A height difference of 0 5 to 1 mm between the centers was found in 42 girls and 36 boys These were evenly distributed among the age groups A height difference larger than one mm occurred in only 4 girls and 6 boys The age of these 10 infants ranged from 2 to 7 months The largest height difference observed in any case was 3 mm

The mean height of the ossification centers according to sex and age is given in Table 3 Although the calculation of these means was based on totally 251 measurements in the girls and 200 in the boys in any infant with bilateral ossification the mean height of both centers was as mentioned treated as a single observation The number of heights analysed statistically was therefore all together 127 in the girls and 107 in the boys

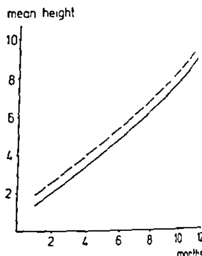


Fig 6 Height (mm) of femoral ossification center according to age in infancy (simplified diagram) Regression lines of both sexes drawn parallel for comparison --- Girls —— Boys

The calculated value of a (eq 2) was 1 24 (SE 0 46) for the girls and 0 49 (SE 0 46) for the boys The calculated value of b was 0 70 (SE 0 06) for the girls and 0 7? (SE 0 06) for the boys The residual standard deviation was estimated as 1 60 for the girls and 1 58 for the boys

Graphs illustrating the mean height of the centers according to age and the regression line are given separately for either sex in Fig 5 which also gives the corresponding 95 per cent prediction intervals F tests revealed no significant deviation from linearity the F value being less than 1 for either sex

Being derived from the measurements obtained in all age groups the linear regression model provides an estimate of the mean height of ossification centers at any age in infancy but this estimate may be less appropriate in the younger age groups in which the fraction of ossified heads was only small

Since the b values for the girls and for the boys proved practically similar the regression lines for both sexes could as well be drawn parallel estimating the value 0 71 for the common slope These lines are compared in Fig 6 which shows a 0 8 month shift of the line for the boys to the right of that for the girls This sex difference in the size of the ossification centers proved significant ($p \sim 0 01$)

Discussion

This department serves all the clinics of a general hospital which is the only hospital in Malmo and its services are reserved for the city population (about 250 000 inhabitants) The material collected for the present investigation would seem an adequate sample of the infants in this population Because of the sampling method employed the ossification had most probably not been disturbed by malformation traumatic injury or disease

It might be assumed that any intrinsic factor involved in the regulation of ossifica

ion will normally operate equally on the right and the left sides This assumption supported by radiologic observations by GROSSMANN He found no difference between the two sides in ossification of the femoral head in 1521 infants In the present material the size of the femoral ossification center was also with but few exceptions similar on both sides The sizes of both centers can therefore not be accepted as independent statistical variates

The few instances of unilateral ossification of the femoral head in the present material were confined to age intervals in which the onset of the ossification of the femoral head is common This suggests that the unilaterality merely reflected the same slight side difference in the rate of ossification as was in some other cases evident from a minor inequality in the size of both centers It should be observed that the sex difference in mean age at the onset of the ossification corresponds fairly well to the delay in the growth of the centers in the boys compared with that in the girls (0 6 months and 0 8 months respectively) The occasional finding of ossification of only one of the femoral heads in an infant below 6 months does therefore not suggest abnormality Multicentric ossification observed in 5 infants in the present series is also probably normal and only transient (SEYSS 1967)

Previous reports about the age of onset and the rate of advance of normal ossification of the femoral head have been widely divergent Some of these were based on only a few observations without mentioning the number and sex of the infants In larger materials the observations have usually been statistically analysed but the methods are often not specified Since even the sampling procedure is frequently not mentioned some materials may have included a substantial proportion of abnormal cases Relatively few investigations have been designed and presented in such a way that the data obtained can be utilized as normal standards in infancy

Most such standards present the fraction of ossified heads according to age thus allowing comparison of for example the mean age at onset of ossification These values are fairly similar in the present material and in that reported by GARN et coll which was a sample of an Ohio born middle-class population Higher values were reported by MOVSHOVICH & VILENSKY and by GUTEZEIT for populations in the Soviet Union and the German Democratic Republic respectively

It is especially interesting to compare the present findings with those made by ELGENMARK in his extensive analysis of the ossification in an assumedly normal material sampled in and around Stockholm during the second World War He found th mean age at the onset of femoral head ossification to be 5 6 months in girls and 4 9 months in boys whereas the corresponding values in the present series are 4 6 and 4 0 months Although both of these Swedish materials may have included some infant members of immigrant families they are not likely to differ significantly in ethnic or genetic respects The marked improvement in the standard of living in the last 30 years might be sufficient to explain the shift towards earlier ossification

Whatever the true explanation may be, the differences found between various materials on record illustrate the importance of defining how and when the reference standards for ossification have been established Minor aberrations of ossification occurring in pathologic conditions may escape recognition unless the normal standards are reasonably contemporary as well as otherwise representative of the population

Acknowledgement

The statistical analysis was carried out by C J Lamm Doctor of Technology

SUMMARY

Observations made in 455 Malmo infants with assumedly normal ossification of the femoral heads were used for establishing reference standards for the age at onset of the ossification and for the size of the ossification centers according to sex and age

ZUSAMMENFASSUNG

Beobachtungen die an 455 Kindern von Malmo bei denen eine normale Ossifikation des Femurkopfes angenommen werden kann wurden verwendet um Referenzstandards fur das Alter beim Auftreten der Ossifikation und fur die Grosse der Ossifikationszentern entsprechend Geschlecht und Alter festzustellen

RESUME

Les observations faites sur 455 nourrissons de Malmo supposés avoir une ossification normale des tetes fémorales ont été utilisées pour établir des étalons de référence pour l âge au début de l ossification et pour les dimensions des centres d ossification en fonction du sexe et de l âge

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were normal in most cases but in those with unilateral dislocation the ossification center of the femoral head on the ipsilateral side was often found to appear later or to be smaller than that on the other side FREDENSBORG who measured the femoral heads on films obtained at the time of his follow up demonstrated that at that age the difference in size between the sides was statistically significant

However the size of the femoral head may even normally differ somewhat with side In 7 of 172 infants aged one to 5 months with no evidence of hip disease an ossification center was found in only one femoral head In 10 of the infants with bilateral centers the height of these differed one to 3 mm with side (PETTERSSON & THEANDER 1979)

LEMPERG et coll (1973) compared the ossification centers at 3 to 12 months of age in 42 infants treated neonatally for unilateral congenital dislocation with those in 98 infants considered to have normal hip joints They measured the height and width of the center on a p films and found that in several instances in either group the sum of these measurements differed by 2 mm or more with side The mean sum was somewhat smaller for the affected side in the infants with dislocation than for those without but when plotted against age the values in the cases with dislocation were found to lie within the range of the others

The present investigation was undertaken to obtain more information on the development of the femoral head in infants treated for congenital dislocation of the hip

Material and Methods

Pelvic films obtained in a sample of the infants treated for congenital dislocation in Malmö in 1966 to 1976 were reviewed This time limit was chosen because radiologic standards for the normal ossification of the femoral head has been established in Malmö infants born in that period (PETTERSSON & THEANDER) The sample of children with dislocation first comprised only those born in 1966 1971 and 1976 but since th boys in this material were too few for statistical analysis it was extended to include also the boys born in 1972 to 1975

The entire sample consisted of 124 infants 81 girls and 43 boys The dislocation was bilateral in 42 girls and 19 boys (Table 1) In all the cases the dislocation had been diagnosed in the first week of life by the following routine which has been continuously applied since 1963

All pregnant women are received for delivery in the General Hospital and every infant is examined by a pediatrician in the morning after birth or exceptionally one or two days later Careful palpation of the hip joints is performed including specific examination of dislocability with the provocation test described by PALMÉN (1961) Th procedure is repeated a few days later before the infant is discharged from the maternity ward If dislocation is evident or suggested the infant is immediately admitted to this department for radiography In all cases with confirmed diagnosis orthopedic treatment is started on the same day

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OSSIFICATION OF FEMORAL HEAD IN INFANCY

II Ossification in infants treated for congenital dislocation

H PETTERSSON and G THELANDER

Classical radiologic descriptions of congenital dislocation of the hip in infants and children stated that the malposition of the femur was accompanied by under development of the acetabulum and femoral head (the Putti triad) These disturbances in osseous growth were believed to be inherent in the disease and the actual dislocation was considered a result of the acetabular dysplasia

However it has later been shown that in congenital dislocation the acetabulum is radiologically normal at birth and that it will remain so if proper treatment is given from the first week of life The development of both the acetabulum and the femoral head may on the other hand be disturbed after birth despite treatment if this has been started too late or is otherwise inappropriate Normal development of the hip in infancy thus seems to require continuous or at most only briefly interrupted maintenance of a truly articulating position of the bones of the joint This concept is consistent with common experience of the consequences of disconnections of othe etiology in various joints e g the hypoplasia accompanying inveterate traumatic or neurogenic dislocation in infancy and it has been supported also by animal experiments (For references see ANDRÉN 1962)

A recent report on 111 children followed 8 years or more after neonatal treatment for congenital dislocation in Malmo confirmed that the hips were invariably clinically normal (FREDENSBORG 1976 a) The hips in these cases have been repeatedly examined in this department As expected the radiologic findings after treatment

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Table 2

Distribution of ossified femoral heads according to side of dislocation in either sex a) before treatment b) 3 months c) 12 months later

		No of ossified heads		Fraction of ossified heads	
		On side with dislocation	On opposite side	On side with dislocation	On opposite side
Girls					
Uni	a)	1	0	0 03	0
lateral	b)	15	23	0 38	0 59
	c)	10	10	1	1
Bi	a)	2		0 02	
lateral	b)	23		0 29	
	c)	18		1	
Boys					
Uni	a)	0	0	0	0
lateral	b)	4	8	0 21	0 42
	c)	5	5	1	1
Bi	a)	0		0	
lateral	b)	5		0 17	
	c)	10		1	

Results

At the initial examination of the 124 infants one had an ossification center in one femoral head and another in both Both were girls they had been examined at the age of one day and 2 days respectively At 3 months of age ossification of the femoral head was observed in 36 of 78 girls and in 11 of 34 boys it was bilateral in 26 of the girls and in 6 of the boys At 12 months of age all of the 29 infants had ossification centers in both femoral heads

The number of infants with ossification of the femoral heads on the various occasions is given separately for unilateral and bilateral dislocation in either sex in Tabl 2 For the cases of unilateral dislocation the distribution according to the side of dislocation is included In these cases the ossification if only unilateral was invariably on the side opposite to that of the dislocation The incidence of ossification in the respective groups in Table 2 is expressed also as the fraction of ossified heads This fraction which is the number of femoral heads with ossification centers divided by the total number of femora in the group was calculated for comparison with the standards for normal ossification

The incidence of ossification before treatment did not differ significantly from normal standards but at 3 months of age the fraction of ossified heads in the cases of unilateral dislocation was above normal in both sexes In the girls the value

Table 1

Distribution of bilateral and unilateral dislocation according to sex in 124 cases diagnosed neonatally and number of infants re-examined in the respective groups 3 and 12 months later

Age (months)	Girls			Boys		
	Bilat	Unilat	Total	Bilat	Unilat	Total
0	42	39	81	19	24	43
3	39	39	78	15	19	34
12	9	10	19	5	5	10

The efficiency of this routine for early detection of dislocation has been evaluated at repeated health controls of all infants and children in Malmo Recent follow up of the children born in 1956 to 1972, altogether 58 759, revealed that among those born after 1965 only 3 cases of dislocation had escaped detection in the first week of life (FREDENSBORG 1976 b)

The radiologic diagnosis of dislocation in the newborn is provided by demonstration of the hip joint while the femoral head is truly dislocated This is achieved by the various manoeuvres and positions described by ANDRÉN (1961) The procedures used invariably include evaluation of the instability of the pubic symphysis (ANDRÉN 1960)

Treatment consists of reducing any actual dislocation and then maintaining the thighs in a position of flexion and abduction for about 3 months using the splint devised by VON ROSEN (1962) As a rule radiography of the hips is repeated immediately after this treatment and on at least one later occasion These examinations are usually confined to an a p view with the thighs extended and adducted Some of the infants with clinically suggested dislocation not confirmed by the initial radiography are treated similarly and repeat examination performed, but no such cases were included in the present series

Repeat radiography was performed in 112 infants at the age of 3 (±0 3) months and in 29 at 12 (±0 5) months The infants examined on either of these occasions are grouped according to sex in Table 1 which also gives the distribution of bilateral and unilateral dislocation before treatment Dislocation was not persistent at the repeat examination in any case

All films taken at the initial examination as well as on later occasions in infancy were reviewed It was noted whether ossification of the femoral head had commenced and, if so, the height shape and structure of the ossification center were evaluated The findings made were compared with the standards for normal ossification obtained from a contemporary sample of Malmo infants (PETTERSSON & THEANDER) Any symphyseal instability at the initial examination was also noted

Table 3

Fraction of ossified heads at 3 months of age according to side of dislocation in either sex and significance of its deviation from the corresponding normal values (0.40 for girls 0.15 for boys)

	Fraction		Significance of deviation	
	Girls	Boys	Girls	Boys
Unilateral				
Side with dislocation	0.38	0.21	None	None
Opposite side	0.59	0.42	p=0.0005	p<0.01
Bilateral	0.30	0.17	None	None

Table 4

Mean (M) and standard deviation (SD) of heights of ossification centers in femoral heads at 3 and 12 months of age in infants of either sex treated for congenital dislocation

	Three months				Twelve months			
	Girls		Boys		Girls		Boys	
	M	SD	M	SD	M	SD	M	SD
Unilateral								
Side with dislocation	1.9	1.75	0.8	1.04	6.6	1.40	6.0	1.17
Opposite side	2.7	1.24	1.8	0.84	7.1	1.32	6.5	1.22
Bilateral	2.8	1.30	2.7	1.28	8.0	2.11	6.3	1.87

estimated from the regression lines established for normal ossification (9.6 mm in girls and 9.1 mm in boys). Assuming a statistically normal distribution this difference was significant ($p<0.01$ for the girls with bilateral dislocation and $p<0.001$ for the other groups).

The height of the centers at 3 months of age was not analysed in this way because in the reference material the centers found in infants younger than 4 months were relatively few. Although the regression lines obtained in that material provide an estimate of the normal mean height throughout infancy, they may be less appropriate at the lower ages (PETTERSSON & THEANDER).

In 22 of the infants found to have bilateral ossification of the femoral head at 3 months of age the right and the left centers differed from each other by more than 0.5 mm in height (17 girls, 5 boys). In 6 of these (5 girls, one boy) the difference exceeded 1 mm. At 12 months of age a difference of more than 0.5 mm with side was found in 12 girls and 7 boys; in 6 and 2, respectively, it exceeded 1 mm. The

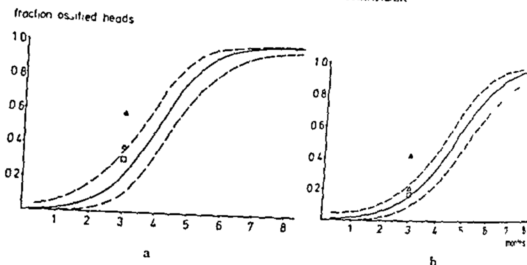


Fig 1 Fraction (f) of ossified femoral heads at 3 months of age in a) girls and b) boys treated for congenital dislocation and logistic model describing the normal variation of f with age Unbroken line logistic curve Broken lines 95 confidence limits of logistic model □ bilateral dislocation △ unilateral dislocation side with dislocation ▲ unilateral dislocation opposite side

found for the side of dislocation decreased slightly and that for the opposite side markedly, outside the 95 per cent confidence interval of the logistic function describing the normal ossification (Fig 1 a) In the boys these values were somewhat lower than in the girls and only that obtained for the side without dislocation fell above the 95 per cent confidence interval (Fig 1 b) In either sex both of the values mentioned were higher than that found in the cases of bilateral dislocation Also this value was above the corresponding logistic curve and more so in the girls than in the boys but did not exceed the 95 per cent confidence limit

The values plotted in Fig 1 were further analysed by comparing their empirical log odds with the corresponding log odds in the logistic models The result is given in Table 3 which shows that the difference in the fraction of ossified femoral heads existing at 3 months of age between the side without dislocation and the normal reference material is statistically significant and more so in the girls than in the boys

The ossification centers of the femoral heads at the initial examination measured 3 0 mm and 3 5 mm in height in the girl with bilateral centers and 1 5 mm in the girl with only one center The size of the centers found in either sex on the two later occasions appears in Table 4 in which the mean heights and standard deviations in the cases of unilateral dislocation are given separately for the side with dislocation and for the opposite side The corresponding values obtained in the cases of bilateral dislocation are also included In these cases the values were calculated in the same way as in the normal reference material i e the mean height of the right and left centers was treated as one observation It appears that on neither occasion was there any statistically significant difference in height between the groups

On the other hand, in all groups distinguished in Table 4 the mean height of the centers at 12 months of age was in each sex smaller than the values for this age

Table 5

Cases with deviations from ordinary shape and structure of ossification centers after treatment

ase o	Sex	Age (months)	Side with dislocation	Height (mm) of centers R	L	Deviation	
	F	3	R L	3 0	2 5	R L	central ossification defect
	F	3	R L	3.5	4 0	R L	central ossification defect
	F	12	R L	7 0	7.5	R L	slightly frayed border
	F	12	R	4 0	5 5	R	biconcave
						L	no deviation
	M	3	R	2.0	2.5	R	irregular structure
						L	no deviation
	M	3	L	3.5	3 0	R L	irregular structure
	M	12	R L	3 0	4 0	R L	irregular shape and structure
	M	12	R L	4 0	4 5	R L	slightly irregular structure

both sides in 5 cases of bilateral and one case of unilateral dislocation In the remaining 2 cases the dislocation had been unilateral and the center on the opposite side was normal Three of these infants were re-examined at 12 months of age (Nos 1 2 5) and 2 at 3 years (Nos 4 7) By then the shape and structure of the centers were invariably normal

The degree of instability of the pubic symphysis demonstrated at the initial examination was 2 3 mm in girls with bilateral and 2 0 mm with unilateral dislocation in boys the corresponding figures were 1 6 mm and 1 7 mm (mean values) It appears that the symphysis was less stable in the girls than in the boys and that no significant difference existed in the degree of instability between unilateral and bilateral dislocation

One girl with bilateral and one with unilateral dislocation had ossification centers in the femoral heads already at the first examination In both of these cases the symphyseal instability (3 0 mm and 3 5 mm respectively) exceeded the corresponding mean values for the girls

The degree of symphyseal instability is shown for various subgroups of either sex in Fig 3 in which the mean values for the infants with and without ossification of the femoral heads at 3 months of age are given for the cases of bilateral dislocation and separately for the sides with and without dislocation in the cases of unilateral dislocation It appears that in all these groups the instability had been greater in the infants with than in those without ossification of the femoral head Since the difference found was only small in each of these groups the ossification at 3 months

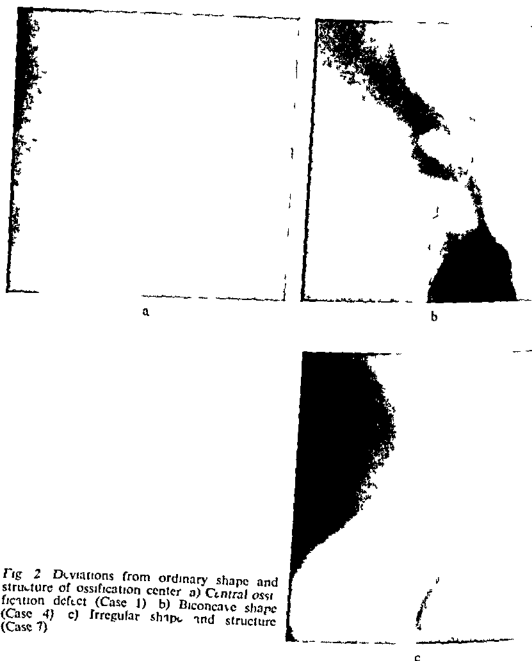


Fig 2 Deviations from ordinary shape and structure of ossification center a) *Central ossification defect* (Case 1) b) Biconcave shape (Case 4) c) Irregular shape and structure (Case 7)

incidence of the difference in height with side was similar in the cases of unilateral and bilateral dislocation At 3 months of age it agreed with the normal standards but, at 12 months differences greater than 1 mm were significantly more common in the infants with dislocation than in the reference *material* *In all* cases of unilateral dislocation the smaller center was on the *same side*

In most of the cases the ossification *centers of the femoral heads* were of *ordinary* shape and structure, but *slight* deviations were found in 8 cases These deviations are briefly described in *Table 5* and are exemplified in Fig 2 They were similar on

an on the other side despite the clinically excellent result of the treatment They o show that a difference in the rate of growth of both centers in such cases per ted throughout infancy As expected these findings agree with those reported by ɪᴇᴅᴇɴsʙᴏʀɢ (1976 a) and with other previous observations in this department

On the other hand it was surprising that at 3 months of age the ossification the femoral head in the cases of unilateral dislocation proved to differ from normal andards not on the same side but on the opposite one The observed acceleration the development on only the side without dislocation can hardly be attributed to e treatment

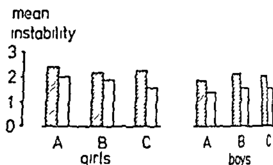
It is therefore noteworthy that in 2 of the 124 cases ossification of the femoral head ıd commenced on one or both sides before the treatment In both cases it is ident from the size of the centers that this ossification had begun already in tero In the reference material ossification centers were never observed in the 84 fants younger than one month and in only 3 of 62 aged one to 2 months Although is difference in incidence is not statistically significant, it suggests that congenital islocation may be associated with accelerated and not as was formerly considered ith retarded development of the femoral head In this context also the instability of e pubic symphysis deserves attention

ᴀɴᴅʀéɴ (1960) stated that in the first few days of life symphyseal instability can e demonstrated in normal infants but is on the average more marked in those ith dislocation He also showed that this is only part of an instability of the pelvis cluding the hips Its degree in infants with dislocation of the hip as well as in ormal infants proved to be higher in girls than in boys probably reflecting a sex ifference in the action of relaxing maternal hormones These and other observations n man together with animal experiments led to the concept of congenital disloca ion being caused by an imbalance of the maternal hormones acting on the pelvis ᴀɴᴅʀéɴ 1962)

The degree of symphyseal instability demonstrated at the initial examination in he present cases in either sex is roughly similar to that reported by ᴀɴᴅʀéɴ in his naterial of congenital dislocation It is noteworthy that the instability was relatively narked in the 2 infants who had already ossification centers in the femoral heads ınd that, 3 months later the infants with marked symphyseal instability proved to ıave such centers significantly more commonly than those with only slight instability The degree of symphyseal instability and its distribution in the present series thus onfirm previous findings and suggest that the hormonal imbalance responsible for the congenital dislocation also tends to accelerate ossification of the femoral head Th assumption of female hormones being responsible for the observed acceleration receives strong support by the significantly earlier normal onset of ossification of the femoral head in girls than in boys

It is evident from common experience with untreated cases that if dislocation persists on on or both sides the acceleration will not prevent marked under development of the corresponding femoral head after birth This underdevelopment

Fig. 3. Neonatal instability of pubic symphysis according to ossification at 3 months of age in various groups of infants treated for dislocation. ▨ infants with, □ infants without ossification centers in femoral heads. A: bilateral dislocation. B: unilateral dislocation, side with dislocation. C: unilateral dislocation, opposite side.



of age was further investigated in the following way for any relationship to symphyseal instability.

Four subsamples of the material were selected according to the degree of symphyseal instability at the initial examination. These consisted of the girls with an instability of 1.5 mm or less, the girls with 3 mm of instability or more, the boys with an instability of 1 mm or less and the boys with 2.5 mm of instability or more. All infants in these subsamples had been re-examined at 3 months of age. The number of infants with ossification centers in one or both femoral heads on that occasion is given for each subsample in Table 6. The χ^2 test with Yates correction revealed that the incidence of ossification in the samples of girls was significantly higher for the one with the higher degree of instability ($p = 0.014$). A similar tendency was found for the boys but here the difference was not significant, probably because of the small samples.

The neonatal instability of the symphysis was also related to the ossification at 12 months of age but the size of the centers at that time did not differ significantly with the degree of instability.

Discussion

The observations made in the present series of neonatally treated cases of congenital dislocation of the hip demonstrate that after unilateral dislocation the ossification center of the femoral head on the ipsilateral side appeared significantly later

Table 6

Incidence of infants with ossified femoral head at 3 months of age in cases of congenital dislocation sampled according to degree of neonatal instability of pubic symphysis in either sex

Sex	Pubic instability (mm)	No. of infants	No. with ossified heads
F	≤1.5	22	5
F	≥3.0	20	13
M	≤1.0	13	2
M	≥2.5	5	3

reduction in size of the epiphyseal bone and accompanying changes in shape and structure (BOHR et coll 1968) These abnormalities closely resemble those in Fig 2

In view of the experiments mentioned and the observations made in cases of congenital dislocation it seems that even the gentle treatment employed in the present series may have slightly impaired the vascular supply to the femoral head If so this impairment was evidently of no clinical significance but it might have contributed to the observed retardation of growth of the ossification center in the femoral head

Acknowledgement

The statistical analysis was carried out by C J Lamm Doctor of Technology

SUMMARY

A review of the films obtained in 124 infants conservatively treated for congenital dislocation of the hip revealed deviations from ordinary development of the femoral head before as well as after the treatment Analysis of these deviations suggested initial acceleration of ossification, modified by retardation ipsilateral to dislocation and followed by bilateral deceleration of growth after treatment

ZUSAMMENFASSUNG

Eine Analyse der Filme die bei 124 Kindern erhalten worden waren die wegen einer kongenitalen Dislokation der Hufte konservativ behandelt worden waren wiesen Abweichungen von der normalen Entwicklung des Femurkopfes bevor sowie nach der Behandlung auf Eine Analyse dieser Abweichungen lassen eine initiale Beschleunigung der Ossifikation vermuten die durch Retardation ipsilateral zur Dislokation modifiziert wird und die von einer bilateralen Verringerung des Zuwachses nach der Behandlung gefolgt war

RESUME

L etude de films obtenus chez 124 nourrissons traites conservativement pour luxation congénitale de la hanche ont montre des deviations par rapport au d veloppement habitel de la tête femorale aussi bien avant qu après le traitement L analyse de ces deviations fait penser qu il y a une accélération initiale de l ossification modifiee par un retard homolateral à la luxation et suivie par un ralentissment bilatéral de la croissance après traitement

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is explained by the actual dislocation Although the dislocation in the present cases was reduced early and definitively it might be assumed to have induced a similar but less severe disturbance of osseous development This would explain why the acceleration at 3 months of age was demonstrable only in the hips that had not been dislocated The systematic occurrence of smaller centers on the side of unilateral dislocation at 12 months of age lends further support to the possibility that the transient dislocation was sufficient to retard local development

The factors discussed offer no explanation why, at 12 months of age the ossification centers of both femoral heads were significantly undersized even after only unilateral dislocation This finding indicates that some further factor or factors exist which unlike the others decelerated the growth of the ossification centers irrespective of the actual dislocation It deserves to be considered whether this deceleration may have been induced by the treatment

Conservative treatment for dislocation in many series on record has been accompanied by more or less severe complications attributed to avascular necrosis The incidence has differed widely and seems to depend on the age at the beginning of treatment and on the procedure employed to reduce the dislocation (FREDENSBORG 1976 a) In some children who had been treated for unilateral dislocation with immobilisation of the hips the abnormalities affected the femoral head on the opposite side suggesting that also this procedure may be responsible for avascular necrosis (FELLANDER et coll 1970)

The treatment in the present series differed from that in many others in two main respects it was invariably started within the first few days of life and the splint applied to maintain proper position of the femoral heads permitted some movement in the hip joints No severe complications have occurred after such treatment in Malmo In his follow up of 111 cases FREDENSBORG (1976 a) found only one hip with radiologic indication of avascular necrosis Even that child was free from symptoms and the abnormalities proved entirely reversible

In the reports of complications minor transient deviations from ordinary shape and structure of the ossification center such as those illustrated in Fig 2 have not usually been taken into account FELLANDER et coll described similar abnormalities in some of their cases of congenital dislocation and considered them as complications Such ossification centers are occasionally found also in the absence of congenital dislocation but they were not observed in the reference material of 455 infants (PETTERSSON & THEANDER) Their occurrence in as many as 8 cases in the present series therefore seems unlikely to be merely coincidental

In experiments in newborn rabbits BOHR et coll (1965) showed that interruption of the vascular supply to the femoral head was followed by transient ischemic necrosis of the epiphyseal bone They found that the ossification process first stopped but was resumed after a few days thanks to revascularisation Examination of the osseous tissue and the zone of enchondral ossification with microradiography and the fluorescence technique in various stages of these events revealed a transient

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BONE MATURATION IN CHILDREN WITH CHRONIC RENAL FAILURE

Effect of 1α-hydroxy vitamin D_3 and renal transplantation

A JOHANNSEN H E NIELSEN and H E HANSEN

Bone age is often retarded in children with chronic renal failure (SCHARER et coll 1976 STICKLER 1976)

As the kidney is the sole site of C-1 hydroxylation the transformation of vitamin D to the biologically active metabolite 1 25 (OH) vitamin D_3 is reduced in these patients (FRASER & KODICEK 1970)

Increased growth and healing of bone lesions have previously been reported to occur in children with renal osteodystrophy when treated with 1 25 $(OH)_2$ vitamin D_3 (CHESNEY et coll 1978) and healing of bone lesions has been demonstrated in children treated with 1α-OH vitamin D_3 (NIELSEN et coll 1977) However no report concerning the effect of 1 25 $(OH)_2$ vitamin D_3 and 1α OH vitamin D_3 on bone maturation in children with chronic renal failure has appeared in the literature

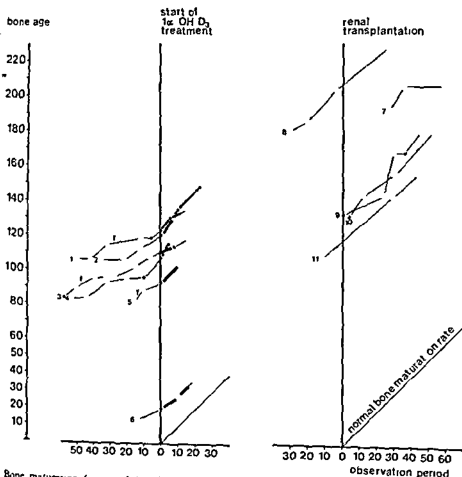
The effects of treatment with 1α-OH vitamin D_3 on bone maturation in children during hemodialysis were analysed and compared with the effect of successful renal transplantation The results are now reported

Material and Methods

The material comprised 11 children aged 2 to 17 years treated at this hospital for chronic renal failure during 1968 to 1977

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Bone maturation (in months) in hemodialysed children before and after treatment with $1\alpha-OH$ vitamin D (Nos 1–6) and in children after successful renal transplantation (Nos 7–11). In case 7 (female) and case 8 (male) the epiphyseal plates closed at the end of observation period (in months). ▼ Renal transplant before $1\alpha-OH-D_3$.

centres and epiphyseal cartilage in the hands and wrists with the standards given in the atlas of GREULICH & PYLE (1959). The figures were related to healthy Danish children who are retarded 6 to 12 months in relation to the North American standard (ANDERSEN 1968, MATHIASEN 1973). Moreover all films of the skeleton were reviewed with regard to renal osteodystrophy.

Results

At the first radiography open epiphyseal plates were found in all patients.

In 5 patients in group 1 (Nos 1–5) aged 8 to 10 years bone maturation was retarded from 6 to 27 months, while normal bone age was found in a one year old child (No 6). Initially this child had marked osteodystrophy, while the other patients in the

Table 1

Clinical data on 11 children with chronic renal failure

Case No	Age on admission (years)	Clinical diagnosis	Period of dialysis (months)	Period of immunosuppressive therapy (months)	Bilateral nephrectomy	Successful renal transplantation
1	10	CPN	64	9	+	-
2	10	CPN	64	0	+	-
3	8	CGN	76	1	-	-
4	10	CGN	56	0	+	-
5	8	CPN	40	1	+	-
6	1	CRD	0	0	-	-
7	15	CGN	3	43	+	+
8	15	CRD	4	27	+	+
9	13	CPN	0	51	+	+
10	13	CGN	2	69	+	+
11	12	CGN	3	30	+	+

CPN – Chronic pyelonephritis CRD – Congenital renal disease CGN – Chronic glomerulonephritis

The patients were classified into two groups (1) Patients treated with 1α-OH vitamin D_3 and (2) patients with a well functioning renal transplant

All children except 2 were treated with hemodialysis for 2 to 76 months (Table I)

The duration of dialysis was 6 hours 3 times per week using a 1 m² 13 5μm thick couprophane membrane (Rhone Poulenc RP5) The dialysis unit was supplied with distilled water and the dialysate contained 3 0 mEq/l of calcium and 1 3 mEq/l of magnesium The patients diet contained 40 to 70 g protein 20 to 30 mEq sodium and 500 to 600 mg calcium per day

The patients in group 1 (5 hemodialysed and 1 non dialysed) were treated with 1α – OH vitamin D_3 for 2 to 22 months (mean 10 7 months) 1α – OH vitamin D_3 was given initially in an oral dose of 1 μg per day for maintaining the level of serum calcium within the upper normal range Serum phosphorus was regulated by aluminium aminoacetate (1 2–3 6 g orally per day) during the period of 1α – OH vitamin D_3 treatment Three patients in this group received a renal transplant before the 1α – OH vitamin D_3 treatment (Figure) The renal transplant never functioned or was rejected in these patients

All 5 patients in group 2 had well functioning renal transplants They were treated with hemodialysis for 0 to 4 months before the transplantation (Table I)

Films of the skeleton were obtained in most patients every 6 to 12 months Children treated with 1α – OH vitamin D_3 were examined both before and after the treatment The bone age was evaluated by comparing the size and shape of the ossification

Table 3

Bone maturation rate expressed as the ratio increase in bone age (months)/increase in chronologic age (months) in hemodialysis patients before and during treatment with 1α − OH vitamin D

Case No	Before 1α − OH − D treatment	During 1α − OH − D treatment	Period of 1α − OH − D_3 treatment (months)
1	0 43	1 27	22
2	0 36	1 11	11
3	0 44	1 50	2
4	0 75	1 00	7
5	0 47	0 50	8
6	0 57	0 70	14
Mean	0 50	1 01	10 7
Range	0 36–0 75	0 50–1 50	2–22

Following transplantation a normal bone maturation rate was attained in all patients (Figure). None of these patients developed radiographic abnormalities suggestive of osteodystrophy.

Discussion

A retarded bone maturation and radiologic signs of renal osteodystrophy were found in children with chronic renal disease as in previous investigations (SCHARER et coll, STICKLER). Although the present results indicate that retarded bone age may occur without radiographic evidence of renal osteodystrophy, abnormal calcium and phosphorus metabolism is probably an important cause of growth failure and renal osteodystrophy in these patients. During treatment with the biologically active 1,25 $(OH)_2$ vitamin D_3 or the synthetic 1α − OH vitamin D_3, the calcium and phosphorus metabolism may become normalized (NIELSEN et coll, CHESNEY et coll.) with subsequent healing of the uremic bone lesions and acceleration of the growth.

However, the effect of these vitamin D metabolites on bone maturation has not previously been described. During the period of hemodialysis the bone maturation rate was reduced and renal osteodystrophy developed. In the period of 1α − OH vitamin D_3 treatment the bone maturation rate was normalized and a marked improvement in the uremic bone lesions—rickets as well as ostitis fibrosa—occurred, as in the series reported by NIELSEN et coll.

Opinions differ about the growth rate in children with renal transplants. GRUSHKIN & FINE (1973) have suggested that growth was poor in transplanted children with bone age corresponding to more than 12 years. However, CHANTLER et coll. (1977) could not confirm this suggestion. In the present series a normal bone maturation rate was found in all patients following successful renal transplantation. The bone age at the first examination indicated that the bone maturation rate had been abnormally low

Table 2

Radiologic bone abnormalities in 11 children with chronic renal failure

Case No	Age at first radiography (months)	Bone age retardation (months)	Radiographic renal osteodystrophy				
			At first examination	In relation to 1α – OH D_3 treatment or successful renal transplant			
				Rickets		Ostitis fibrosa	
				Before	After	Before	After
1	130	15	–	–	–	–	+
2	120	6	–	+ +	+	+ +	+
3	102	9	+	–	–	+ +	+
4	121	27	–	+	–	+ +	+ +
5	104	10	–	+ +	+	+ +	+
6	13	0	+	+ + +	+	+ + +	–
7	198	0	–	–	–	–	–
8	190	0	–	–	–	–	–
9	166	23	–	–	–	–	–
10	166	25	–	–	–	–	–
11	154	36	–	–	–	–	–

group only had varying degrees of halisteresis but no characteristics indicating renal osteodystrophy (Table 2)

In the period of hemodialysis before 1α – OH vitamin D_3 treatment bone retardation became more marked in all patients in group 1 (Figure) The bone maturation rate expressed as bone age/chronologic age was found to be 0 36 to 0 75 (Table 3) Five of the 6 patients developed renal osteodystrophy during this period No relation was found between the severity of the renal osteodystrophy and the bone maturation rate The bone disease was no more prominent in patients in whom bilateral nephrectomy was performed than in children with the kidneys in situ

During the period of treatment with 1α – OH vitamin D_3 the bone maturation rate was normal (Figure Table 3) Moreover, the bone lesions markedly improved in the 5 patients with renal osteodystrophy both with regard to the rickets and the ostitis fibrosa However in the patient without evidence of renal osteodystrophy before administration of 1α – OH vitamin D_3 slight abnormalities indicating ostitis fibrosa were apparent at the examination following treatment (Table 2)

In group 2 normal bone age was observed in 2 patients (Nos 7, 8) aged about 16 years at the first radiography, while bone age in the other children (Nos 9-11) aged 12 to 13 years was retarded 23 to 31 months (Table 2) All the patients had a slight degree of halisteresis The patients received a well functioning renal transplant shortly after the first radiography therefore only few data concerning bone age before surgery are available (Figure)

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in the period before transplantation in the younger but not in the older patients. The normal bone maturation following renal transplantation might be due to improved renal function with production of 1 25 (OH) vitamin D_3 the kidney being the sole place of C – 1 hydroxylation necessary for the transformation of vitamin D into the active metabolite (FRASER & KODICEK)

It is concluded that 1α – OH vitamin D_3 treatment as well as successful renal transplantation may normalize the bone maturation rate in children with chronic renal failure

Acknowledgements

1α – OH vitamin D_3 was kindly supplied by Leo Pharmaceutical Products Copenhagen Denmark

SUMMARY

In 8 of 11 children with terminal chronic renal failure bone age was retarded 6 months to 3 years During hemodialysis the bone maturation rate decreased 1α – OH vitamin D_3 treatment and renal transplantation normalized the bone maturation rate

ZUSAMMENFASSUNG

Bei 8 von 11 Kindern mit herabgesetzter Nierenfunktion war das Knochenalter 6 Monate bis 3 Jahre verspatet Während Hämodialyse sank die Knochenreifungsrate Mit 1α – OH Vitamen D_3 Behandlung und Nierentransplantation normalisierte sich die Knochenreifungsrate

RÉSUMÉ

Chez 8 enfants sur 11 atteints d insuffisance rénale chronique terminale l age osseux était en retard de 6 mois à 3 ans Pendant l hémodialyse la vitesse de maturation osseuse a diminue Le traitement par la vitamine D_3 1α – OH et la transplantation rénale ont normalisés la vitesse de maturation osseuse

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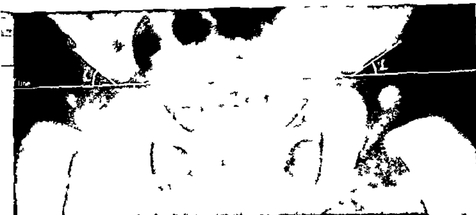


Fig 1 Two-month-old girl The right hip joint is unstable with retarded skeletal development of the iliac bone and the femoral head The Y line is drawn The most cranio-lateral and caudo-medial parts of the ilium in the acetabulum are marked with dots on both sides α 43 5 right and 34 left

tion now reported was performed in order to assess the value of measuring the acetabular angle in infants with idiopathic hip instability diagnosed after the neonatal period The instability was corroborated by arthrography in all cases

Definitions

Unstable hip joint A hip joint in which the femoral head is or can be moved out of the acetabulum partially or completely

Acetabular dysplasia Abnormal ossification of the iliac bone (roof of acetabulum) observed at conventional radiography of the hip The chondral part of the acetabulum may appear normal or abnormal in shape at arthrography

Neonatal period The first month of life

Material and Methods

The material consisted of a consecutive series of 29 children (27 girls 2 boys) with idiopathic hip instability The age ranged at the time of diagnosis between 1½ and 12 months In all cases the diagnosis was confirmed by arthrography In 28 children the instability was unilateral 19 left sided and 9 right sided and bilateral in one girl thus in all 30 unstable and 28 stable hips After closed reduction of the unstable hip joint the legs were kept in abduction for 13 to 29 weeks generally in plaster The length of treatment depended on the age of the child at diagnosis on the degree of instability as estimated at the initial arthrography and on clinical observation during the treatment period After treatment all hips were clinically stable A

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HIP JOINT INSTABILITY AFTER THE NEONATAL PERIOD

I. Value of measuring the acetabular angle

B. ALMBY and T. LÖNNERHOLM

HILGENREINER (1925) introduced the concept of Pfannenwinkel (acetabular angle or acetabular index) as a method of estimating the development of the acetabulum. He used this angle among other radiologic criteria to establish the diagnosis of hip instability in infants. The normal value was estimated to be about 20°. The acetabular angle (α) in unstable hips was observed to be twice as large.

Since that time the acetabular angle has been used extensively in clinical practice. However, its value for diagnosis of hip instability in the newborn has been seriously questioned by many authors (CAFFEY et coll. 1956, ANDRÉN & VON ROSEN 19.., PALMÉN 1961).

Normal values for the acetabular angle in children of different ages after the neonatal period have been presented by many authors (e.g. KLEINBERG & LIEBERMAN 1936, FABER 1937, MASSIE & HOWORTH 1950, DÜR 1953, CAFFEY et coll. 1956, WILKINSON & CARTER 1960, ZIPPEL 1971). An extensive and thorough analysis of the normal values has been presented by TÖNNIS & BRUNKEN (1968). They emphasized the importance of a correct position of the pelvis for adequate reproducibility. They also demonstrated differences in the normal values of the angle between girls and boys and between the right and left hip. Opinions are still divergent about the values (KELLER 1975, KRISTEN et coll. 1976, TÖNNIS 1976). The investiga-

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Fig. 3 Girl 5 months old at diagnosis Left sided instability α 25 5 right and 39 3 left The points needed for calculation of the angle of inclination of the pelvis are marked on os ischium and pubis on both sides This angle (∀) is 125 The width of the right obturator foramen (9 mm) divided by that of the left one (12 mm) gives the index of rotation of the pelvis (0 75)

means the position of the pelvis could be controlled at each examination with reference to a rotation index and an angle of inclination respectively The rotation index was determined by measuring the greatest width of the right and left obturator foramen on the film along a line parallel to the Y line and forming the ratio between these values (Fig 3) The angle of inclination (the symphysis—os ischium angle) is the angle between two lines connecting the most cranio-medial part of os ischium with the most cranial part of the superior ramus of the pubis close to the symphysis (Fig 3)

The acceptable ranges of variation for the rotation index which are reported to be 0 56 to 1 8 and for the angle of inclination which are reported to be 96 to 135 for children aged one to 12 months and 92 to 128 for children one to 3 years old were taken into account here All measurement points were marked on transparent paper over the film on a viewing table The accuracy of the angle measurements was about 0 5

For comparison of the measurements made by the two observers the entire material was used When comparing the acetabular angles with the normal values the two boys and one girl in whom the lateral rotation and the inclination of the pelvis were outside the permitted limits of variation were excluded

The material was grouped by age as described by TÖNNIS & BRUNKEN (Table I Figs 4 5 6) From the normal values given by TÖNNIS & BRUNKEN for the right and left hips in girls common values were calculated (mean SE SD) for the two sides (Table I Figs 4 5 6)

Statistical methods Conventional methods (HOEL 1971) were used for calculating mean values standard deviations (SD) and standard errors of the mean (SE)



Fig 2 Girl 12 months old Left unstable hip For the calculation of α the caudal part of the ilium on the Y line is first marked Because of the markedly retarded ossification of the iliac bone 2 points are marked in the bony acetabular roof—one medial and one lateral From the 2 angles ∢ (40) and ∢ (29) α is calculated to be 34 5 (40 + 29)/2

clinical and arthrographic analysis of 20 of these children is reported elsewhere (ALMBY & LÖNNERHOLM 1978)

In all children conventional films of the hips were exposed before treatment and within 5 weeks after termination of the abduction therapy Each examination included at least two a p views of the pelvis one with the legs in the neutral position and one with the legs in maximum abduction At the first examination a test of stability was also performed in which the legs were extended rotated inward and pressed axially The film demonstrating the least lateral rotation of the pelvis was chosen for the measurements On all 58 films (29 before treatment and 29 after) bilateral measurement of the acetabular angle (α) was performed by the two authors independently A line Y was drawn at a tangent to the caudal border of the ilium on both sides (Fig 1) The most cranio lateral point of the acetabulum and its most caudo medial point on the ilium were marked and a line was drawn between these two points The angle (α) between this line and the Y line was measured (Fig 1) In cases in which an abnormal skeletal development of the acetabulum made it difficult to determine the cranio lateral measurement point two points were determined (Fig 2) Thus two angles were obtained for which the mean was calculated and designated α in these cases The acetabular angle in each hip (mean for the two observers) was compared with the normal values given by TÖNNIS & BRUNKEN

Pelvic measurements as recommended by TÖNNIS & BRUNKEN for determination of the lateral rotation and the inclination of the pelvis were performed By this



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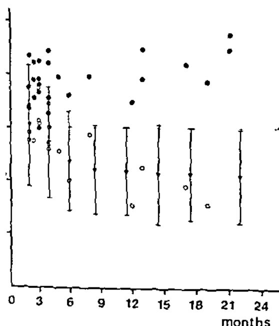


Fig 4 The individual acetabular angles (α) in 26 girls (52 hips) before treatment and the mean acetabular angles ± 2 SD in normal girls of different age groups The 2 transverse dotted lines at 30 and 50 mark the variation of α in dislocated hips as reported by SCHWARTZ ● = unstable hips present material ○ = stable hips present material ▼ = mean values in normal hips from TONNIS & BRUNKEN

After treatment the acetabular angles were reduced in all cases The difference tween the previously unstable hip and the stable hip was reduced to less than 5 16 of the 22 cases diagnosed before the age of 7 months In 6 of these the angle the previously unstable hip was even smaller than that of the stable hip Two the 6 unilateral cases diagnosed after 7 months of age still had angular differences more than 10 The girl with bilateral instability had persistently large angles The normal values for the acetabular angle for girls and in the present series of ls in different age groups appear in Table 1 Before treatment it is evident how e acetabular angles of the unstable hips remained at about 30 to 50 with advancing e (Figs 4 5) while the angles of the stable side became smaller over the same riod as in the normal hips After treatment the angles in the previously unstable ps diminished and even reached the normal values except in the age groups over 5 months and in the group 13 to 16 months (one child) The values for the stable ps were normal in all age groups

Discussion

At conventional radiography in newborns with idiopathic instability of the hip no ssification disturbances in the hip joint can be demonstrated either they are absent r so slight as to escape discovery (SALTER 1966) Thus from this standpoint radio raphy in the neonatal period is not worthwhile A special radiographic method

Table 1

Average acetabular angles (α) in normal girls with stable hips (reported by TÖNNIS & BRUNKEN) *and in girls with hip instability (present series) before and after treatment*

Age group	Age (months)	Girls with stable hips		Girls with hip instability					
				Before treatment			After treatment		
		No of subjects	α (left and right) ±SE	No of cases	α±SE		No of cases	α±SE	
					Stable hips	Unstable hips		Stable hips	Unstable hips
I	1–< 3	25	30 3±1 1	7	29 8±1 4	38 2±1 4			
II	3– 5	90	27 1±0 6	10	28 6±1 7	36 8±1 7			
III	5–< 7	96	23 7±0 5	2	22 8±2 8	37 5±1 8	3	20 7±2 6	[illegible]8 14
IV	7–< 10	143	22 1±0 4	1	28 5	39 3	12	19 1±1 1	[illegible]10±1[illegible]
V	10–< 13	84	21 8±0 5	1	15 5	34 5	4	15 9±2 7	17 8 [illegible]
VI	13–< 16	62	21 2±0 6	2	20 5±2 0	41 6±2 9	1	21 5	[illegible]6 0
VII	16–< 19	44	21 3±0 7	1	19 0	41 5	1	13 0	[illegible]0 0
VIII	19– 25	59	20 9±0 6	2*	15 5	43 2±2 6	3	14 3±0 8	[illegible]8 0 [illegible]
IX	25– 37	59	18 8±0 5				2*	1[illegible] 0	34 0±[illegible]
				Σ = 26			Σ = 26		

* One case with bilateral hip instability

Significances of differences between mean values were calculated by Student's t test The statistical significance (p) was tested at the 0 01 level

Results

The mean difference ± SE between the acetabular angles obtained by the two observers appear in Table 2 The difference is expressed in degrees for 4 group – stable and unstable hips before and after treatment The mean difference was about 0 25° in 3 groups A significant difference (less than 2) was found only for the unstable hips before treatment The maximum individual difference was 5 stable and 8° in unstable hips

Before treatment the angle of the unstable hip was greater than on the stable side in all unilateral cases The difference was 10 or more in 8 of the 22 infants diagnosed before the age of 7 months and more than 10 in all 6 unilateral cases diagnosed after this age The angles in the girl with bilateral instability were among the greatest in the series In 2 stable hips acetabular dysplasia (Fig 7) was diagnosed in the others no skeletal abnormalities existed

The ranges of the acetabular angles are given in Table 3 The angle values in stable and unstable hips overlapped considerably in infants below the age of 7 months

Table 2

The mean difference ± SE (in degrees) between the values for the acetabular angles obtained by the two observers in measuring the acetabular angles (α) in the series The statistical significance (p) was tested at the 0.01 level

	No of hips	Mean difference ± SE	Significance
Stable hips			
At diagnosis	28	0 27 ± 0 30	No
After treatment	28	0.21 ± 0 38	No
Unstable hips			
At diagnosis	30	1 83 ± 0 36	p < 0 01
After treatment	30	0 18 ± 0 30	No

Table 3

The acetabular angles (α) before treatment in 29 children Range (in degrees) in two age groups

Age at diagnosis (months)	Unstable hips		Stable hips	
	α	No of hips	α	No of hips
1 5–< 7	28 5–44 3	22	18 5–37 5	22
7–< 12	34 5–47 0	8	15 5–28 5	6
		Σ = 30		Σ = 28

of cases hip instability present in the neonatal period disappeared spontaneously within 2 months

The acetabular angle is an index of the development of the acetabulum and has been attributed great importance in the literature for the diagnosis of acetabular dysplasia By having two independent observers measure the acetabular angles in both stable and unstable hip joints an idea was obtained of the reliability of such measurements In measuring stable hip joints the average difference between the two observers was negligible In unstable hips it was clearly more difficult to define the measurement points in the acetabulum Significantly different values were recorded in individual hip joints but on the average the difference did not exceed 2 This figure may therefore be regarded as a reasonable measure of the accuracy when one series of patients is compared with another

The normal values of acetabular angles given by TÖNNIS & BRUNKEN are based on a German material They agree well with those reported by WILKINSON & CARTER The normal acetabular angle is somewhat greater on the left side than on the right (TÖNNIS & BRUNKEN) The differences varied from 0 6 to 2 2 in girls of different age

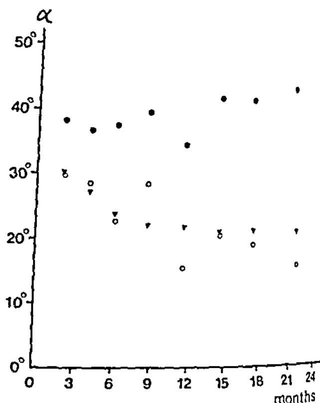


Fig. 5. The mean acetabular angles (α) for 26 girls in eight different age groups before treatment. Symbols as in Fig. 4.

of demonstrating instability in the newborn has been described by ANDRÉN & VON ROSEN. However, clinical examination alone is generally considered sufficient to establish a diagnosis (PATTERSON 1976, among others).

After the neonatal period radiography is an important aid in diagnosing hip instability. Nowadays in Sweden the few cases with a late diagnosis are generally detected as early as at one to 6 months of age (PALMÉN 1977). As the clinical signs of hip instability (restricted abduction, etc.) may be difficult to evaluate at this age, radiography is often of decisive importance for the diagnosis. Diagnostic difficulties at radiography arise mainly in cases in which the femoral head has not begun to ossify, making its position difficult to assess. This is especially true when the instability is only slight. Films exposed during a provocation manoeuvre may then be of value.

That deficiencies in the ossification of the acetabulum and femoral head occur in the presence of persistent instability is well known. Abnormalities may be observed in the lateral part of the ilium as early as at a few weeks of age (FELLANDER et coll. 1970, KELLER). Retardation of acetabular ossification should therefore give reason to suggest instability of the hip.

Minor deficiencies in the acetabular ossification were present in 2 stable hip joints with normal arthrography. The abnormality had disappeared and the ossification was entirely normal after a further 5 months of observation. This is in conformity with the observations of BARLOW (1962), who reported that in a number

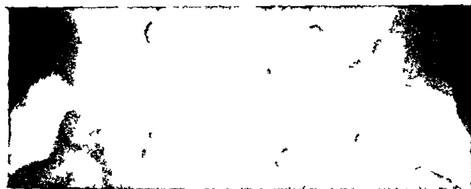


Fig. 7 Girl 3 months old at diagnosis Right sided hip instability at arthrography The skeletal development in the acetabulum is retarded on both sides in the lateral part of the iliac bone α 39 right and 37 5 left

least 10 before it may be regarded with certainty as indicating pathologic conditions in the hip with the greatest angle

It was found in the present series that the mean acetabular angle in unstable hips in the respective age groups differed significantly from the normal values (Table 1) This indicates that measurement of the acetabular angle is of value in comparing two populations

In the assessment of the development of a hip in an individual patient the acetabular angle is of value After treatment this angle is lower (Fig 6) but in children diagnosed and treated after the age of 18 months the reduction was less marked than that observed at a lower age This observation is in line with those made by SALTER and SCHWARTZ that the potential of the acetabulum for normal development tends to decrease greatly after this age HARRIS (1976) however gives 4 years as the corresponding age limit A contributory cause of the slow development of the acetabulum in the late cases may be residual instability that is not observable clinically but can be diagnosed by arthrography (ALMBY & LÖNNERHOLM)

Conclusions

(1) Several series of normal values have been presented in the literature The values given by TÖNNIS & BRUNKEN compare well with those in the present material

(2) The mean difference between the acetabular angles recorded by the two observers was greater in unstable than in stable hips but did not exceed 2

(3) *In all* unstable hips disturbances in the skeletal development of the acetabulum were observed In children with unilateral instability the acetabular angle was always greater *on the* unstable side

(4) The acetabular angles on the two sides must differ by at least 10 before a definite *difference* in development can be considered to exist A minor difference

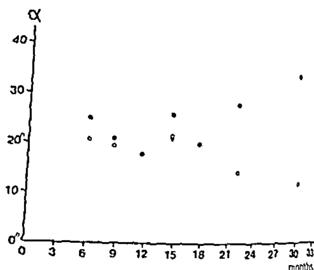


Fig 6 The mean acetabular angles (α) in 26 girls in different age groups after treatment Symbols as in Fig 4

groups These minor differences were disregarded by KRISTEN et coll as well as in the present investigation The values given by TÖNNIS & BRUNKEN have been criticised as *being too high* in the youngest age groups (KELLER KRISTEN et coll) *in the group* of one to 3 months they are based on a number of infants (75) considered too small However in view of the fact that TÖNNIS & BRUNKEN excluded cases with extreme pelvic positions established *on the basis of firm* criteria their material *must be regarded* as the most reliable normal material TÖNNIS & BRUNKEN state *that the* acetabular angle is affected by a maximum of 2° by the permitted lateral rotation of the pelvis and by a maximum of 3° by permitted pelvic inclinations.

At a pace with the *ossification of the* acetabulum, the acetabular angle diminishes with *increasing age* In the presence of hip instability this is not the case In more *than 300* girls aged between 6 months and 3 years and 9 months with dislocation *of the hip* GROSSE (1939) found a mean angle of 42 5° with a mean variation of less *than 3°* between different age groups SCHWARTZ (1965) *found the individual angle to be 30 to 50° in 50 cases of* hip dislocation diagnosed between 4 months and 5 *years and 4 months* The present series exhibited similar conditions (range 28 5–47).

TÖNNIS & BRUNKEN state that only definitely pathologic hips are grouped above *the limit formed* by the mean value + 2 SD From *Fig 4 it is evident that their limit for* definitely pathologic *cases of ages* above 6 months coincides approximately with *the lower limit for* pathologic variation (30) found by SCHWARTZ On the other hand *in the lower ages* the normal variation (i e values within the mean value ± 2 *SD) are partly found* within the pathologic limits *given (30–50) As a* diagnostic criterion of acetabular dysplasia *the method* is therefore uncertain at these ages if the values in the individual case *are to be* compared with normal tables

In the present series the *acetabular angle* was always *greater on the* unstable than on the stable side This was true even in the youngest children If consideration is paid to the *influence of* various factors (position of *pelvis errors of* measurement and normal variation between left and *right hip)* an angular difference must be at

ns ayant une instabilite unilaterale l angle acetabulaire etait toujours plus grand du coté stable Cette difference diminue après le traitement Les auteurs discutent les critères des igles pathologiques Le mesure de l angle acetabulaire a un très grand interet pour juger :ffet du traitement mais a une utilite limitee pour diagnostiquer l instabilité en particulier :ndant les 6 premiers mois de la vie car la composante cartilagineuse des articulations est pas incluse dans la mesure L arthrographie est conseillee dans les cas difficiles à juger

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does not exclude a pathologic development but cannot alone form the basis of a diagnosis of acetabular dysplasia

(5) On diagnosis of hip instability during the first 6 months of life the acetabular angle does not always give sufficient information Other criteria such as a lateral ossification defect and a double contour in the acetabulum or both must therefore be relied upon

(6) Skeletal acetabular abnormalities can occur in the absence of instability Arthrography is of value in deciding whether instability is present or not when the clinical findings are uncertain

(7) After the first 6 months of life an acetabular angle exceeding 30° is invariably pathologic

(8) The acetabular angle is a simple measure of the skeletal development of the acetabulum during and after therapy and is also a suitable parameter for comparing different series of patients

SUMMARY

The acetabular angle was measured by two independent observers in a consecutive series of 29 infants with idiopathic instability of the hip The diagnosis was made at the age of 1½ to 21 months and was confirmed by arthrography The average difference in the measurement values between the two observers was less than 2° In infants with unilateral instability the acetabular angle was always greater on the unstable side This difference decreased after treatment Criteria for pathologic angles are discussed Measurement of the acetabular angle is of greatest value for assessing the effect of treatment but is of limited usefulness in diagnosing instability especially during the first 6 months of life as the cartilaginous component of the joint is not included in the measurement Arthrography is recommended in cases difficult to evaluate

ZUSAMMENFASSUNG

Der Winkel des Acetabulum wurde zwei Untersuchern in einer aufeinanderfolgenden Reihe von 29 Kindern mit idiopathischer Instabilitat des Huftgelenks gemessen Die Diagnose wurde bei einem Alter von 1½ bis 21 Monaten gestellt und durch Arthrographie bestatigt Die durchschnittliche Differenz in den Messwerten bei den beiden Untersuchern war geringer als 2 Bei Kindern mit unilateraler Instabilitat war der Winkel des Acetabulum stets grosser auf der instabilen Seite Dieser Unterschied wurde geringer nach der Behandlung Kriterien der pathologischen Winkel werden diskutiert Die Messung des Acetabularwinkels ist von grosstem Wert um den Effekt der Behandlung festzustellen Sie ist jedoch von begrenztem Wert die Diagnose der Instabilitat zu stellen besonders wahrend der ersten Lebensmonate da die Knorpelkomponente des Gelenks nicht von der Messung erfasst wird Arthrographie wird in zweifelhaften Fallen empfohlen

RÉSUME

L angle acétabulaire a été mesuré par deux observateurs indépendants sur une série consécutive de 29 nourrissons atteints d instabilite idiopathique de la hanche Le diagnostic a été fait à l age de 1½ à 21 mois et a été confirmé par arthrographie La différence moyenne des valeurs mesurées par les deux observateurs a été inférieure à 2 degrés Chez les nourris

IOM THE DEPARTMENTS OF ORTHOPAEDIC SURGERY (DIRECTOR PROF T HIERTON) AND IAGNOSTIC RADIOLOGY (DIRECTOR PROF H LODIN) AKADEMISKA SJUKHUSET S 750 14 UPPSALA SWEDEN

HIP JOINT INSTABILITY AFTER THE NEONATAL PERIOD

II The acetabular growth potential

B ALMBY S GREVSTEN and T LÖNNERHOLM

The newborn infant has an average acetabular angle (index) of 25 to 31 (KLEINBERG & LIEBERMAN 1936 FABER 1937 ZSEBÖK et coll 1952 CAFFEY et coll 1956 COLEMAN 1956 STANISAVLJEVIC 1962) when measured as recommended by HILGENREINER (1925) In the first year of life the angle decreases continuously—to about 20 in boys and 22 in girls at 12 months of age (TÖNNIS & BRUNKEN 1968) During the rest of the growing period the reduction proceeds more slowly to 14 in boys and 15 5 in girls at 7 years of age (TÖNNIS & BRUNKEN)

In children with idiopathic hip joint instability diagnosed after the neonatal period the development of the acetabular angle lags behind the normal (KLEINBERG & LIEBERMAN GROSSE 1939 HILGENREINER 1939 ZSEBÖK et coll SCHWARTZ 1965 TÖNNIS & BRUNKEN ALMBY & LÖNNERHOLM 1979) If the hip is successfully reduced the development will begin again and will tend to normalize if the duration of the instability has not been too long

It has been discussed (SCHWARTZ SALTER 1966 HARRIS et coll 1975 HARRIS 1976) at what age this tendency to acetabular growth diminishes or vanishes thereby making normal development impossible It is of practical interest in this connection to consider the most appropriate time for different operative procedures undertaken to prevent deterioration of the hip

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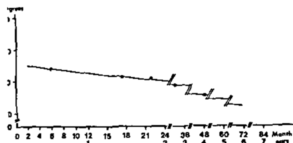


Fig 1 Normal values for the acetabular angle (α_n) of girls in different age groups are marked with dots The values common for the right and left hip joint are calculated from figures reported by TÖNNIS & BRUNKEN The function $\alpha_n(t) = e^{0\,01\;t\;3\;4}$ based on these data is marked as a line (The age groups reported by TÖNNIS & BRUNKEN are given in the Table)

he lateral rotation and inclination (tilt) of the pelvis were within the limits given by TÖNNIS & BRUNKEN

The girls were divided into groups according to the age at diagnosis and after treatment as recommended by TÖNNIS & BRUNKEN (Table) The mean of the normal values for the left and right hip for girls as given by TÖNNIS & BRUNKEN was calculated and represents the normal value irrespective of side (Table Fig 1)

Further details about the measurements of the acetabular angle and the position of the pelvis are reported in Part I (ALMBY & LÖNNERHOLM 1979)

Methods of calculation The fast development of the hip joint of the infant in the first year of life runs parallel with the rapid general growth in that period It thus seems justifiable to assume that the development of the acetabular angle (α) follows the generally accepted formula for biologic growth

$$f(t) = e^{k_0\;t\;a_0} \tag{1}$$

where f(t) is the biologic quantity at time t k_0 and a_0 are constants
Applied to the angular development

$$\alpha\,(t) = e^{k_1\;t\;\;1} \tag{2}$$

where α (t) is the angle established at time t k_1 and a_1 are constants

With regard to the acetabular angle in the unstable hip (α_u) it is known that it constantly lies above 28 (ALMBY & LÖNNERHOLM 1979) Higher values have been found with increasing age (GROSSE SCHWARTZ among others) This relation is approximated to a linear function

$$\alpha_u = k_2\;t + a_2 \tag{3}$$

where α is the angle of the unstable hip at time t k_2 and a_2 are constants

A function describing the difference between the pathologic angle and the normal one would however give a better information of the disturbed development at a certain age

The present series of unstable hips covers age groups which parallel age groups in reports for normal hips (TÖNNIS & BRUNKEN) The difference between the acetabular

Table

The mean acetabular angle (α) ± SE (standard error of the mean) in degrees in different age groups in the present material of 26 girls with 27 unstable hips at diagnosis and after treatment The values for normal girls are calculated from figures reported by TÖNNIS & BRUNKEN

Age groups	Age (in months)	Present material at diagnosis		Normal girls		Present material, after treatment	
		No of cases	α±SE	No of subjects	α±SE	No of cases	α±SE
I	1– 3	7	38 2±1 4	25	30 3±1 1		
II	3– 5	10	36 8±1 7	90	27 1±0 6		
III	5– 7	2	37 5±1 8	96	23 7±0 5	3	24 8±1 4
IV	7–<10	1	39 3	143	22 1±0 4	12	21 0±1 7
V	10– 13	1	34 5	84	21 8±0 5	4	17 8±0 5
VI	13– 16	2	41 6±2 9	62	21 2±0 6	1	26 0
VII	16–<19	1	41 5	44	21 3±0 7	1	20 0
VIII	19–<25	2*	43 2±2 6	59	20 9±0 6	3	28 0±4 8
IX	25– 37			59	18 8±0 5	2*	34 0±7 8
X	37– 61			33	15 6±0 7		
XI	61 85			24	15 5±0 8		

* One bilateral case

In this report a mathematical analysis of the normal development of the acetabular angle its arrest in unstable hips (diagnosed after the neonatal period), and the potential towards normality after treatment are presented (For definitions see Part I p 201)

Material and Methods

The material consisted of a series of 26 girls with idiopathic hip instability In 25 children the instability was unilateral 17 left sided and 8 right sided and bilateral in one girl, thus in all 27 unstable hips The diagnosis was made at the age of 1 5 to 1 months and was in all cases confirmed by arthrography After closed reduction all hip joints were immobilized for 13 to 29 weeks generally in a conventional hip spica plaster The age at diagnosis and the degree of instability determined the length of the period in plaster After treatment all hips were clinically stable

In all children conventional films of the hips were exposed before and within 5 weeks after termination of the treatment Each examination included at least two a p views of the pelvis The film demonstrating the least lateral rotation of the pelvis was chosen for the measurements On all 52 films (26 before treatment and 26 after) measurement of the acetabular angle of the unstable hip(s) was performed by two of the authors independently (B A and T L) The mean of the angles measured by the two observers was also calculated and was used for the mathematical analysis In all films

atment differential These values varied between 2 2 and 5 7 a month with a mean 3 2 in the cases where treatment was started before the age of 14 months but only tween 0 6 and 1 5 , with a mean of 1 1 in the cases where treatment was started ter This is illustrated in Fig 2 where the slope of the lines expresses the rate of duction

It is apparent from Fig 2 that no simple age related rate of angular reduction exists cases where treatment was begun before 14 months—i e treatment begun at 3 onths of age for example did not necessarily reduce the angle at a higher rate than eatment starting 5 months later Even in girls within the same age group the rate of duction of the angle during treatment differed Above the age of 14 to 16 months eatment resulted in a much slower progression of the skeletal acetabular development than when it was started earlier

Discussion

Basically two factors are to be considered as regards the acetabular development hen planning treatment for unstable hip joints One is how much the acetabular ngle differs from the normal one at the age when the treatment is to start and the ther is how great is the potential of the acetabulum to normalize i e how rapidly ill it reduce its angle towards the normal one

The time it takes to normalize can be estimated approximately by the formula

$$t = \frac{w}{s}$$

where t = time w = way s = speed in this particular case $w = \alpha_d$ (Fig 4) s = reduction of α per month

Assuming a monthly reduction of about 3 at ages of up to 14 months it is quite imple to deduce from Fig 4 an average treatment period at different ages

At the age of three months ($\alpha_d = 10\ 5$) for example a period of treatment of four months seems adequate at the age of 12 months ($\alpha_d = 16$) at least five months of treatment and so on

The individual differences will of course give treatment periods of variable lengths but an analysis as described will nevertheless give an indication of the duration of treatment required

With regard to treatment starting above the age of about 14 to 16 months two facts are to be kept in mind—one that there is a long way to go and the other that the pace seems to be slower This slower pace is expressed both in the normal function (Fig 1) the gradual decline in the angular decrease and in the treatment differential (Fig 2) The findings in children above the age of 16 months substantiate the observation by SCHWARTZ and SALTER that the age of about 18 to 20 months would seem to be an upper limit for definite successful treatment by conservative means only

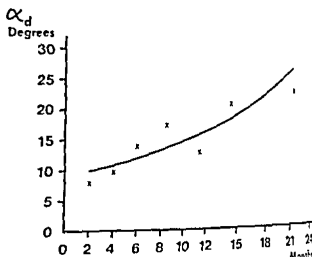


Fig 4 The mean of the differences (α_d) between the normal acetabular angle (α_n) and the mean of the acetabular angles of unstable hips (α_u) in the different age groups is marked with X The function $\alpha_d(t) = e^{0\,0\ \ t\ \ 17}$ based on these data is marked as a line

about 38 and at 19 to 25 months at about 43° The method of least squares gav a linear regression (non logarithmic) with the following formula

$$\alpha_u(t) = 0\ 3\ \ t + 35\ 9$$

$$r_{\alpha_u t} = 0\ 71$$

suggesting a slightly increasing acetabular angle from two to 22 months in the un stable hip joints (Fig 3)

Retardation of the acetabular development in unstable hip joints related to the normal values of Tonnis & Brunken According to eq (4) and the discussion follow d concerning methods of calculation the difference between the acetabular angle in unstable hip joints and that in normal hip joints in corresponding age groups r presents the retardation in development of the acetabular angle in the unstable hip joints at a particular time of diagnosis Applying the method of least squares to thes differences the following function was obtained

$$\alpha_d(t) = e^{0\,0\ \ t\ \ 17}$$

$$r_{\alpha_d t} = 0\ 87$$

This function shows increasing values (Fig 4) implying that an abnormal acetabular angle diagnosed at the age of for example 12 months when therapy is begun h s greater decline to make if normality is to be achieved than the same angle value at 2 months A difference in the development retardation thus exists between these tw age situations The intention in constructing this function was to determine how the gap between a normal and an unstable hip joint increases with age

Change in acetabular angle in the unstable hips during treatment In order to evaluate the rate at which the individual angle decreased during the treatment period th angular reduction during this was divided by the length of the period—giving th

..tabular growth potential in these hip joints and normal ones is presented During treat nt the monthly reduction of the acetabular angle is greater than in normal hip joints The limit for sole treatment in immobilisation without operative procedures is discussed

ZUSAMMENFASSUNG

Bei 26 Madchen mit idiopathischer Huftgelenksinstabilitat die nach der Neonatalperiode ignostiziert worden war wurde der Winkel des Acetabulum vor und nach der Behandlung messen Eine mathematische Analyse des Wachstums Potentials des Acetabulum bei diesen d normalen Huftgelenken wird gegeben Wahrend der Behandlung ist die monatliche ..rminderung des Acetabularwinkels grosser als bei normalen Huftgelenken Die Alters nze fur die Behandlung durch Immobilisation ohne operative Verfahren wird diskutiert

RESUME

Les auteurs ont mesuré l angle acetabulaire avant et apres traitement chez 26 filles ayant le instabilité idiopathique de l articulation de la hanche diagnostiquee après la période onatale Ils presentent une analyse mathématique du potentiel de croissance acetabulaire ir ces hanches instables et sur les hanches normales Pendant le traitement la reduction ensuelle de l angle acétabulaire est plus grande que dans les hanches normales Les auteurs scutent l age limite pour un traitement uniquement par immobilisation et sans intervention hirurgicale

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The development potential of the pathologically retarded acetabulum is of greater magnitude than the normal one (Figs 1 2) The reason for this accelerated growth is not known but it seems to start as soon as the femoral head has been concentrically reduced and stabilized in this position

The differences in the degree of instability between the different hip joints that are easily demonstrated at arthrography, are perhaps one reason for the differences in the rate at which the retarded acetabulum tends to normalize As noted previously (ALMBY & LÖNNERHOLM 1978) this might be the explanation for the slow progress in the older children where a slight residual instability was still present even after more than 6 months in plaster, when a second arthrography was performed

When applying the formula $\alpha_n = e^{0.01 t + 3.4}$ normal values were obtained for girls one to 5 months old which are somewhat lower than those presented by TÖNNIS & BRUNKEN for these ages (Fig 1) but are in good agreement with values recently published by SCHUSTER (1978) According to KRISTEN et coll (1976) the angles reported by TÖNNIS & BRUNKEN are too high for the ages before 6 months This might be due to difficulties in distinguishing between normal infants of these ages and infants with retarded growth (acetabular dysplasia) in whom a slight idiopathic neonatal instability (not diagnosed) may have stabilized leaving the acetabular growth for some months behind The formula mentioned corrects for this thereby giving lower values as it is mainly based on observations made at ages of about 6 months onwards

Conclusions

(1) The normal development of the acetabular angle (α_n) in girls can be expressed as a biologic growth function $\alpha_n = e^{0.01 t 3.4}$

(2) The angle α_n has a decline which is greatest during the first year of life and gradually diminishes up to the age of 7 years

(3) The retarded acetabular development in unstable hip joints related to the normal growth can be expressed by the formula $\alpha_d = e^{0.0 t 17}$

(4) The acetabular development following the treatment is faster than the normal It amounts to about 3 a month when treatment is started before the age of 14 months

(5) After the age of about 14 to 16 months both the normal and the treatment induced acetabular developments are slower than at earlier ages This age might constitute the limit at which closed treatment is successful without further procedures or extreme periods of immobilisation

(6) By using a simple diagram (Fig 4) it is possible to estimate the average duration of closed treatment required for different ages

SUMMARY

In 26 girls with idiopathic hip joint instability diagnosed after the neonatal period the acetabular angle is measured before and after treatment A mathematical analysis of the

tabular growth potential in these hip joints and normal ones is presented During treat nt the monthly reduction of the acetabular angle is greater than in normal hip joints The limit for sole treatment in immobilisation without operative procedures is discussed

ZUSAMMENFASSUNG

Bei 26 Madchen mit idiopathischer Huftgelenksinstabilitat die nach der Neonatalperiode gnostiziert worden war wurde der Winkel des Acetabulum vor und nach der Behandlung nessen Eine mathematische Analyse des Wachstums Potentials des Acetabulum bei diesen d normalen Huftgelenken wird gegeben Wahrend der Behandlung ist die monatliche rminderung des Acetabularwinkels grosser als bei normalen Hüftgelenken Die Altersnze fur die Behandlung durch Immobilisation ohne operative Verfahren wird diskutiert

RESUME

Les auteurs ont messure l angle acetabulaire avant et apres traitement chez 26 filles ayant le instabilité idiopathique de l articulation de la hanche diagnostiquee après la periode onatale Ils presentent une analyse mathématique du potentiel de croissance acetabulaire r ces hanches instables et sur les hanches normales Pendant le traitement la reduction ensuelle de l angle acetabulaire est plus grande que dans les hanches normales Les auteurs scutent l age limite pour un traitement uniquement par immobilisation et sans intervention irurgicale

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TRIPHALANGISM AND PSEUDOTRIPHALANGISM OF THE THUMB IN CHILDREN

G THEANDER and N CARSTAM

A thumb with three phalanges in a row is uncommon in man but the malforma ion has been known for centuries and as early as in 1907 more than a hundred uch thumbs could be collected from the literature (HILGENREINER) This abnor nality is called triphalangism to distinguish it from another type of malformation in which a supernumerary phalanx and one of the ordinary phalanges are instead ituated side by side such phalangeal duplication is regarded as incomplete poly lactyly Triphalangism of the big toe seems to be extremely rare

Although most reports on triphalangism concern only single cases several families are on record in which members of one or more generations have had a triphalangeal humb on one side or both (HILGENREINER 1910 HAAS 1939 LAPIDUS et coll 1943 ABRAMOWITZ 1967 and others) Triphalangism seems to be most often a solitary malformation but it may be associated with other anomalies

Duplication of one or both thumbs and other types of polydactyly for example have been found both in persons with triphalangism and in their relatives (MILCH 1951 KOMAI et coll 1953) Families reported by KOMAI et coll and by PHILLIPS (1971) had various malformations of the feet as well as of the hands including triphalangeal thumbs Concomitant malformations may involve the radius (KELIKIAN 1974) or the tibia (PASHAYAN et coll 1971) Triphalangism of the thumb is a component of two recently discovered specific malformation syndromes (AASE & SMITH 1969 TOWNES & BROCKS 1972) and it has been found also in some cases of the Holt

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Table

Sex age at radiography and at operation and diagnosis in 10 cases of malformation of the thumb
F female M male R right L left N normal TP triphalangism PTP pseudotriphalangism

Case No	Sex	Age at radiography	Age at operation	Diagnosis R	Diagnosis L
1	F	6 y 10 y 14 y	14 y (R L)	TP	TP
2	M	16 y	No operation	TP	TP
3	F	6 y	9 y (R) 10 y (L)	TP	TP
4	M	8 m 13 m	13 m (L) 7 y (R)	TP	TP
5	F	4 d	No operation	TP	N
6	F	19 m 3 y	3 y	TP	N
7	M	7 m 16 m	No operation	TP	TP
8	F	17 m 9 y 10 y	10 y (R)	TP	PTP
9	F	8 y	8 y (R)	PTP	PTP
10	M	6 y	6 y	N	PTP

Oram syndrome (ZETTERQVIST 1963 EMERIT et coll 1965) and in a case of trisomy 13–15 (POZNANSKI et coll 1971)

A triphalangeal thumb is more or less disabling depending mainly on its morphology which may differ considerably from one case to another The individual morphology is important also because this must be considered in the selection of cases suited for surgical treatment in the choice of reconstructive procedures and in deciding the age at which operation should be carried out Adequate pre operative classification of triphalangism is therefore desirable as a guide to proper therapy

A type of malformation of the thumb resembling triphalangism but with only one interphalangeal joint has been observed at this hospital This abnormality is here called pseudotriphalangism The experience gained from such cases and from the series of truly triphalangeal thumbs have facilitated pre operative differential diagnosis of each type of malformations and allowed recognition of significant variation in either type A clinically useful classification based on the radiologic appearances is now described Clinical diagnosis and surgical procedures will not be discussed but pertinent observations made at operation are included

Material and Methods

The material consisted of 4 boys and 6 girls with triphalangeal or pseudotriphalangeal thumbs examined between 1961 and 1977 Both hands were affected in 7 cases One boy had slightly dysplastic shoulder and elbow joints (Case 2) One girl admitted to this hospital at 6 years of age with bilateral duplication of the thumbs had 5 years previously been treated elsewhere with removal of the rudimentary supernumerary digits (Case 3) In the other cases no concomitant malforma

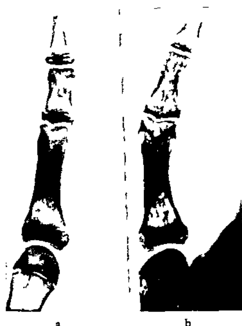


Fig 1 Triphalangeal thumbs simple variety P a views a) Case 1 left thumb at 14 years b) Case 2, right thumb at 16 years Middle phalanges similar to those in normal triphalangeal fingers Long first meta carpal Curved base phalanx in (b)

ion was discovered but in Case 1 the father was said to have some malformation of the hand One mother had taken thalidomide during the pregnancy (Case 4)

Radiography of the 17 abnormal thumbs was performed at least once at ages ranging from 4 days to 16 years and 10 were operated upon Four of the cases have been previously mentioned in a report on surgery of clinodactyly (CARSTAM & THEANDER 1975)

The films were reviewed in 1977 in the light of observations made at operation and the anomalies were classified according to the radiologic appearanc s

Results

The radiologic appearances of the 17 malformed thumbs suggested triphalangism in 13 and pseudotriphalangism in 4 of these digits The diagnoses in the individual cases are specified in the Table which also gives the sex and the ages at which the radiography and the operations were performed Bilateral triphalangism was dia gnosed in 5 cases and bilateral pseudotriphalangism in 1 case Of the remaining 4 children 2 had a triphalangeal right and a normal left thumb whereas 1 had a normal right and a pseudotriphalangeal left thumb In one case the right thumb was tri phalangeal and the left pseudotriphalangeal

Observations made at operation of 8 of the triphalangeal and 2 of the pseudo triphalangeal thumbs corroborated these diagnoses The other 7 thumbs were not surgically explored but all of these could be firmly classified by the radiologic appearances alone One thumb of a girl first examined at 17 months of age could



Fig 2 Triphalangeal thumbs LBD variety a) Case 5 right thumb at 4 days lateral view b) Case 6 right thumb at 19 months p a view Short and skew middle phalanges malaligned with other phalanges Ulnar clinodactyly Structural abnormality of middle phalanx in (b) indicating ossification anomaly (LBD)

not be classified with certainty at that time but pseudotriphalangism was evident at radiography 8 years later (Case 8)

The radiologic appearances of triphalangism are illustrated in Figs 1 2 3 a and 3 c and those of pseudotriphalangism in Figs 3 b 3 d 4 and 5 The following varieties were distinguished

Triphalangism

In 7 triphalangeal thumbs referred to in the following as the simple variety the middle phalanx resembled the ordinary middle phalanx of any normal triphalangeal digit (Fig 1) In the other 6 the middle phalanx was strikingly skew in shap and position (a so called deltaphalanx) causing marked clinodactyly of the end phalanx (Figs 2 3 c) The radiologic appearance of these middle phalanges was consistent with a special ossification anomaly that has been more commonly found in other tubular bones of the hands and feet Such abnormal ossification was described as longitudinally bracketed diaphysis (LBD) in a previous report concerned with its various sites and its radiologic features in different stages of growth (THEANDER & CARSTAM 1974) Consequently the thumbs with a middle phalanx with these features are for convenience here called the LBD variety In both varieties operation confirmed that the middle phalanx articulated with the other phalanges

The simple variety Thumbs with the simple variety of triphalangism were found bilaterally in Cases 1 2 and 3 and on the right side in Case 4 The length of the middle phalanx relative to the length of the other phalanges of the thumb differed somewhat from one case to another but with this exception the shape and structure of the middle phalanx were essentially similar in all the thumbs A proximal epiphysis existed which at all ages proved to be in the same stage of ossification as in the middle phalanges of other digits

The thumbs in this variety deviated to the ulnar side because of a slope of the distal joint surface of the middle phalanx but this clinodactyly of the end phalan



Fig 3 Triphalangism (LBD variety) and pseudotriphalangism Case 8 a) Right b) left thumb at 7 months lateral views Small abnormal ossicle interposed between base phalanx and diaphysis of end phalanx on both sides c) Right d) left thumb at 10 years p a views Middle phalanx only in right thumb In left thumb oversized skew epiphysis of end phalanx Ulnar clinodactyly less marked on left side

was only slight (Fig 1 a) In Case 2 however the right thumb had a marked ulnar deviation which was due mainly to an abnormal slope of the proximal interphalangeal joint This slope was in turn explained by a curvature of the base phalanx with its concavity on the ulnar side (Fig 1 b) In all cases a distal accessory ossification center or its residue was found in the first metacarpal which was strikingly long

The LBD variety This variety of triphalangism was found in the left thumb in Case 4 in the right in Cases 5 6 and 8 and bilaterally in Case 7 Since these children were not examined at the same age the radiologic appearance of the middle phalanx differed with the stage of the abnormal ossification An osseous bracket extending separately along one side of the diaphysis and uniting the epiphyseal ossification center with a distal center as previously demonstrated in some other children was less obvious in this series of thumbs but in those examined at 17 months of age or later a structural abnormality suggesting LBD was recognized in the middle phalanx (Figs 2 3c) Skewness and a lopsided position of the abnormal phalanx as well as clinodactyly which are other characteristic features of LBD were evident independently of age in all the cases At no age was a separate epiphyseal ossification center of the middle phalanx demonstrable in this variety An accessory distal ossification center of the first metacarpal was found in all cases examined at 19 months or later The clinodactyly was invariably to the ulnar side

The middle phalanx in Case 8 did not extend along the entire corresponding joint surface of the other phalanges thereby permitting these to articulate with each

other on the ulnar side (Fig 3 c) In the other cases the distance between the base and end phalanges suggested two entirely separate joints between these and the middle phalanx

Pseudotriphalangism

In the pseudotriphalangeal thumbs the proximal part of the end phalanx contained an abnormal osseous element which could be and in one case initially was mistaken for a middle phalanx Such thumbs were found bilaterally in Case 9 and in the left hand in Cases 8 and 10 Their radiologic appearances differed in all of these cases and hence deserve individual description

Case 8 Both thumbs were found at 17 months of age to have a small abnormal ossicle between the base phalanx and the diaphysis of the end phalanx The distance of this ossicle to the base phalanx was similar on both sides but its distance to the diaphysis of the end phalanx was somewhat smaller in the left thumb (Fig 3 a b) The site of the ossicle on the left side resembled that of an ordinary endphalangeal epiphysis but no other digit in either hand had an end phalanx with an epiphyseal ossification center Such phalangeal centers were present only in the base phalanges of the 2nd to 4th fingers in both hands and these centers were much smaller than the abnormal ossicles in the thumbs Both thumbs were therefore assumed to be triphalangeal

At re examination 8 and 9 years later the abnormal ossicle in the right thumb had assumed more characteristic features of the LBD variety of triphalangism (Fig 3 c) but evidently no middle phalanx existed in the left thumb An epiphyseal ossification center had in the meantime appeared in the base phalanges of both thumbs and in the end phalanx of the right thumb but not in the left It was thus obvious that the abnormal ossicle in the left thumb had not really been supernumerary as initially thought but was instead the extreme premature epiphyseal ossification center of the end phalanx It had remained oversized and had become larger on its radial than on its ulnar side This skewness caused a slight slope of its metaphyseal surface and a corresponding deviation of the diaphysis to the ulnar side (Fig 3 d) The first metacarpal in either hand had a distal accessory ossification center

Case 9 Both hands were found at 8 years of age to have ordinary separate ossification centers in their tubular bones except in the end phalanges of the thumbs An accessory distal ossification center existed bilaterally in the first metacarpal In either thumb a skew osseous element articulated with the distal end of the base phalanx causing ulnar clinodactyly This element was not quite equal in size or shape on both sides but at least in the right thumb it resembled a rudimentary middle phalanx Yet its position on each side suggested that it belonged to the end phalanx (Fig 4) At subsequent operation on the right thumb a wedge including adjacent portions of the abnormal bone element and of the diaphysis of the end phalanx was resected No joint space was detected between these two portions

Case 10 The left hand examined at 6 years of age had a normal epiphyseal ossification center in the base phalanx of the thumb and in the first metacarpal which had also an accessory distal center The epiphysis of the end phalanx of the thumb contained a bipartite osseous element One of the two portions had the appearance of a roughly normal epiphyseal ossification center except that the radial part of its proximal surface seemed to be in osseous continuity with the other portion which was somewhat smaller and wedge shaped causing ulnar clinodactyly Both portions appeared to articulate jointly with the base phalanx (Fig 5 a)





Fig 4 Fig 5

Fig 4 Pseudotriphalangeal thumbs Case 9 p a views a) Right b) left thumb at 8 years Epiphyseal osseous part of end phalanx simulating rudimentary middle phalanx bilaterally Ulnar clinodactyly

Fig 5 Pseudotriphalangeal thumb Case 10 Left thumb at 6 years p a views a) pre operatively Supernumerary wedge shaped ossicle incompletely fused with ordinary ossification center of end phalanx Ulnar clinodactyly b) During operation Ossicle ex cised Intraarticular air separated from base phalanx by joint cartilage but in close contact with epiphyseal bone in end phalanx

Operation confirmed the osseous continuity between both epiphyseal portions of the end phalanx and also that both were covered by a continuous articular cartilage After resection of this cartilage the wedge shaped osseous portion was excised A film was exposed after these stages of the operation which was then immediately completed with reduction of the clinodactyly and reconstruction of the soft tissues Since air had entered the joint space during the operation the absence of epiphyseal cartilage at the site of excision was evident on this film, whereas at the distal end of the base phalanx the air outlined the surface of a normal articular cartilage (Fig 5 b)

Discussion

HILGENREINER who surveyed the cases of triphalangism on record by 1907 made a basic distinction between single and double thumbs and subdivided the former category into 4 groups according to the morphology of the phalanges Group I was described as incomplete (unvollstandig) hyperphalangism group II as complete but imperfect (unvollkommen) and group III as perfect hyperphalangism In group IV a supernumerary ordinary triphalangeal finger was thought to have replaced the thumb The appearances of the bones in the respective groups were illustrated by drawings which however cannot be regarded as conclusive evidence of a true difference between groups III and IV The drawings exemplifying these two groups

closely resemble the findings made in those of the present cases referred to here as the simple variety of triphalangism

Although the drawings shown by HILGENREINER do not clearly illustrate the structure of the middle phalanx the descriptions given of the thumbs in his group II seem consistent with LBD which had at that time not yet been recognized as a characteristic ossification anomaly It appears likely that the LBD variety of triphalangism distinguished in the present series corresponds entirely to his group II

Group I in the survey mentioned comprised only 4 out of 68 thumbs diagnosed as hyperphalangeal single thumbs These 4 thumbs had been found in adults and none of them contained more than 2 separate osseous elements They were thus obviously only biphalangeal but the end phalanx was relatively long and its cortex had a slight transverse or oblique indentation which was considered suggestive of incomplete hyperphalangism A subsequent report on additional cases included a girl aged 15 months with abnormal thumbs which were also assigned to group I (HILGENREINER 1910) Her thumbs had a supernumerary osseous element which judging from the illustrations resembled a cone epiphysis of the end phalanx Yet also this ossicle was continuous with the endphalangeal diaphysis at the top of the cone The present cases of pseudotriphalangism seem to be the first in which an entirely separate ossicle simulating a middle phalanx has been observed

The grouping used by HILGENREINER has not become widely applied but a distinction has since been commonly made between opposable and nonopposalbe triphalangeal thumbs This important difference in functional ability depends on various factors such as the condition of the muscles and other soft tissues and of the metacarpophalangeal joint but it seems to be related also to the morphology of the phalanges Most opposable triphalangeal thumbs on record have been similar to the present ones of the LBD variety whereas nonopposable thumbs have usually resembled those referred to here as the simple variety However as pointed out by KELIKIAN (1974) phalangeal morphology offers no reliable clue to the range of motility which should be evaluated clinically rather than radiologically

Also etiologic classification might be attempted on the basis of certain observations The familial occurrence and the association of triphalangism with other malformations mentioned are valid arguments for hereditary disturbances of development but alternative causes are known to exist e g thalidomide given to the mother during the pregnancy (LENZ et coll 1964) However there seems to have been no close relationship between the morphology and the causative factors In the present series the coexistence of one triphalangeal and one pseudotriphalangeal thumb in Case 8 as well as the combination of both varieties of triphalangism in Case 4 strongly suggest that these malformations reflect a protean expressivity of a common developmental disturbance rather than different etiologies

As exemplified by some of the present cases the morphology in either type of malformation may differ with the stage of ossification Since specific differences in the radiologic appearance with age have been shown to exist in LBD at various

s (THEANDER & CARSTAM) it was not unexpected to find some of these differences o in the LBD variety of triphalangism But it was surprising that in Case 8 the phalan ism which was at the first examination thought to be bilateral later proved have been spurious on one side The similarity of both thumbs at the first amination in this case is striking and on that occasion only attention to the slightly fferent sites of the right and left abnormal ossicles might have afforded a radiologic ue to the adequate diagnoses on both sides

In later stages of growth pseudotriphalangism would seem less likely to be mis ken for true triphalangism and after ossification has become completed there will obably never be any doubt whether a thumb is bi or triphalangeal Also differential agnosis between the two varieties of triphalangism is likely to become easier with dvancing age but in pseudotriphalangism individual differences in morphology may nd to decrease as ossification proceeds It is possible that the bipartite bone ele ient found in Case 10 and the simple endphalangeal ossicl bilaterally in Case 9 and i the left thumb in Case 8 reflect the existence of two permanently different varieties f pseudotriphalangism but it cannot be excluded that they may represent successive tages in th abnormal ossification of the end phalanx Further experience is ecessary to elucidate this point

The clinical importance of distinguishing triphalangeal from pseudotriphalangeal humbs would seem evident and also the value of preoperative discrimination e tween both varieties of triphalangism can hardly be questioned In pseudotri phalangism distinction b tween varieties would for the reasons mentioned be premature but even in this malformation the individual morphology has in fact as mentioned in the case histories already prompted the use of different surgical procedures It thus appears likely that awareness of the morphologic variation will be rewarding in the treatment of both types of malformations

SUMMARY

In 10 children with altogether 17 malformed thumbs radiography revealed true triphalang ism in 13 of the thumbs and pseudotriphalangism in the remaining 4 Two varieties of triphalangism were distinguished and clinically significant morphologic variation was recog nized also in pseudotriphalangism

ZUSAMMENFASSUNG

Bei 10 Kindern mit insgesamt 17 verbildeten Daumen ergab die Rontgenuntersuchung Triphalangismus in 13 der Daumen und Pseudotriphalangismus in den ubrigen 4 Zwei verschiedene Arten von Triphalangismus wurden unterschieden Eine morphol gische Varia tion von klinischer Bedeutung kam auch bei Pseudotriphalangismus vor

RÉSUMÉ

Chez 10 enfants ayant au total 17 pouces malformés la radiographie a montre un vrai triphalangisme sur 13 de ces pouces et un pseudo-triphalangisme dans les quatre autres Deux variétés de triphalangisme ont été distinguées et une variation morphologique clinique ment significative a été reconnue dans le pseudotriphalangisme

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RADIOLOGY OF THE EAR IN MANDIBULO FACIAL DYSOSTOSIS—TREACHER COLLINS SYNDROME

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The appearances and clinical features of mandibulo facial dysostosis and their relationship to other first arch syndromes have been fully described (WARKANY 1971 KELEMEN 1974 GORLIN et coll 1976) Many patients have a bilateral conductive deafness with or without external meatal atresia although cochlear function is almost always normal It is only recently that some understanding of the aetiology of the condition has been brought about by animal experiments (POSWILLO 1975 b) and discrimination made from other facial and aural abnormalities such as hemifacial microsomia which may have very similar ear deformities

However few descriptions of the type of ear deformity which occurs in mandibulo-facial dysostosis have appeared Treacher Collins original description of two cases makes no mention of ear abnormalities or deafness and his illustration seems to show a normal pinna (COLLINS 1900) These were presumably mildly affected cases FRANCESCHETTI & KLEIN (1949) whose names are also given to this syndrome gave a comprehensive review These authors state that there may be abnormalities of external middle and inner ears They describe the microtia and deformity of the pinna as well as the short blind-ending external auditory meatus but attempt no description of the middle and inner ear lesions beyond mention of diploeic mastoids These observations are based on the Stenvers projection and histologic material is not presented Nearly all cases are described as having middle ear deafness although no audiometric details are given

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Table

Degree of atresia of middle and external ears in mandibulo-facial dysostosis

Case No	Atresia of attic and antrum		Atresia of external auditory meatus		Other features
	Right	Left	Right	Left	
1	+ +	+	—	—	Narrow sloping external meatus no ossicles
2	+	+	+	+ +	Small mobile ossicles on the right (operation) probably none on the left
3	+	+	+	—	Deformed ossicles
4	+ +	+ +	+ +	+	Very dilated lateral semi-circular canal no ossicles narrow hypotympanum anterior n VII
5	+	+	+ +	+	Slightly dilated tilted lateral semi-circular canal ossicular mass right and probably left
6	+	+	—	—	Normal eardrums ossicles present but deformed right n VII adherent to mobile stapes (operation)
7	+ +	+	+ +	+	No ossicles identified anterior n VII both sides
8	+	+	+	+ +	Ossicles present malleus and incus fused to the atretic plate on the left (operation)
9	+	+	—	—	Normal eardrums ossicles present but deformed right n VII adherent to fixed malleus (operation)
10	+	+	+	+ +	Anteriorly placed ossicular mass on the left no ossicles on the right
11	+		—	—	Sloping curved external auditory meatus with eardrums present ossicles present on the right and probably on the left
12	+ +	+ +	—	—	Curved external auditory meatus but normal eardrums ossicular remnant probably attached to roof of attic

TERRAHE (1972) described the reduction in size of the middle ear cavity and especially the attic and antrum with deformed or often absent ossicles Recently HUTCHINSON et coll (1977) described the appearance of the middle ear cavities and ossicles in 16 patients with mandibulo facial dysostosis These descriptions seem to be based mainly on tomographic appearances but there are no illustrations Depression of the tegmen was found in 13 of the 32 ears The only observed inner ear abnormality occurred in one patient in whom the left ear demonstrated an abnormally shaped vestibule and lateral semi circular canal

Material and Results

Twelve cases were considered to be true examples of mandibulo facial dysostosis The degree of atresia of the middle and external ears appear in the Table All cases had the typical facial appearances with deformed low slung pinnae and bilateral



Fig 1 Con-avity of the inferior edge of mandible which is typical of mandibulo-facial dysostosis

conductive deafness in the 50 to 80 dB range In every case the attic and antrum were reduced in size and the tegmen displaced inferiorly Three patients had a positive family history two had cleft palates and one a pre auricular sinus Although all patients had normal cochlear function tomography demonstrated minor deformities of the lateral semi-circular canal in two cases

Seven other cases which had at some time been labelled as Treacher Collins did not conform to the characteristics of this syndrome and were therefore excluded although the ear lesions were similar These patients 5 with unilateral and 2 with bilateral ear lesions were considered to be examples of hemifacial microsomia The ear lesions tended to be more bizarre the descent of the tegmen and middle fossa dura was often more marked and in a few cases there was hyperplasia of bony structures derived from tympanic and styloid apparatus rather than the hypoplasia seen in mandibulo-facial dysostosis Moreover the jaw deformities were different from those characteristically present in mandibulo-facial dysostosis (Fig 1) In the bilateral cases of hemifacial microsomia both jaw and ear lesions were markedly asymmetric whereas in mandibulo-facial dysostosis only slight differences existed between the two sides (Fig 2)

In 5 patients the external auditory meatus was of normal calibre on each side but tended to slope upwards to a normal tympanic membrane (Fig 3) Four ears in this series were explored In 2 the ossicles were considered to be normal although probably rather small in one case In the other 2 ears the malleus was fixed and the incus reduced to a small flake of bone in one the stapes had a single strut In both these ears the facial nerve was abnormal and dehiscent being stuck to the malleus in one and to the stapes in the other



Fig 2 External auditory meatus which run upwards and are curved but of normal calibre Mastoi On the right some deformed ossicles (→) fused to the low tegmen Coronal section at the level of the oval windows



Fig 3



Fig 4

Fig 3 Small slit like attic extending horizontally (→) External auditory meatus runs almost vertically (↔)

Fig 4 A shelf of bone in place of the attic (→) Base section at the level of the cochlea (c) passin through internal (i) and external auditory meatus

Discussion

The description of any type of ear deformity depends ultimately on histologic section Probably because the majority of children with mandibulo facial dysostosis grow up and live normal lives few temporal bones have been examined histologically Conventional ear radiography as used in previous descriptions is inadequate for assessing the middle ear lesions which occur in this syndrome However multidirec tional tomography when used in a reasonably large series and compared with the findings at surgery post mortem and with animal models demonstrates a distinctive range of deformities



Fig 5 Fig 6

5 Greatly reduced attic (→) with an ossicular mass Section at the level of the cochlea
;. 6 Thick atretic plate with facial nerve canal (f) anteriorly placed Tegmen is very low Only a middle ear cavity (→)

The most obvious and constant feature is an underdeveloped and unpneumatised astoid combined with a varying degree of atresia of attic and antrum (Fig 4) ie external auditory meatus is often narrow or may be completely or partially retic Even if the meatus is of normal calibre it tends to run upwards from the low ing and deformed pinna

The ossicles are almost always abnormal when the middle ear cleft is reduced lalleus and incus may be fused together or to the walls of the narrow attic (Fig 5) deformity of the malleus and incus can be easily recognised on the tomograms and ision to form an ossicular mass often predicted However fusion to the walls of ie middle ear cavity is much more difficult to assess and deformities of the stapes nd discontinuity at the incudo-stapedial junction cannot usually be identified In pontaneously occurring congenital ear lesions the typical ossicular mass is often arger than the combined size of a normal malleus and incus but in mandibulo-facial lysostosis the deformed ossicles are of normal or reduced size

The course of the facial nerve is usually abnormal the degree of aberration ap pearing to depend more on the meatal than on the attic atresia (Fig 6) The nerve ollows a more direct path laterally from the geniculate ganglion This means that the descending part may run more or less horizontally and it is usually more an teriorly positioned than normal This part of the facial nerve canal runs through solid bone as there are no mastoid air cells present in mandibulo-facial dysostosis It can therefore be easily recognised on coronal or lateral tomograms although a dehiscent segment in the middle ear and absence of a mastoid process may mean that this bony canal is short The extent of forward displacement can usually be assessed on coronal sections by considering the position of the descending part in relation to the labyrinth and in particular the oval window if this is present (PHELPS et coll 1977)

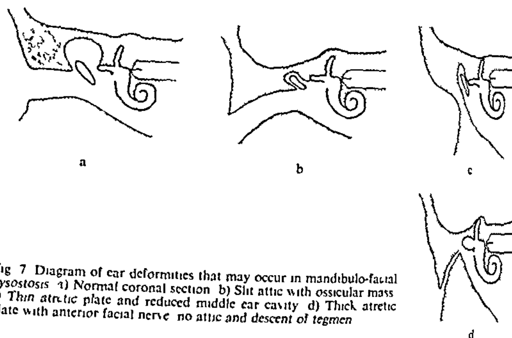


Fig 7 Diagram of ear deformities that may occur in mandibulo-facial dysostosis a) Normal coronal section b) Slit attic with ossicular mass c) Thin atretic plate and reduced middle ear cavity d) Thick atretic plate with anterior facial nerve no attic and *descent of tegmen*

Cochlear function is nearly always normal in these children and consequently the cochlea has a normal shape with a normal curl of the modiolus demonstrated by *coronal tomography* The only inner ear deformity in the present series involved the lateral semi circular canal In two cases this was shorter and wider than normal (Fig 7 d) This is the commonest inner ear anomaly demonstrated by tomography and has been described in mandibulo facial dysostosis by several authors (SANDO et coll 1968 PHELPS 1974 HUTCHINSON *et coll*) *It is found also in* craniofacial dysostosis thalidomide embryopathy anencephaly and chromosome trisomy abnormalities It may also be an incidental finding

There is a consistency of the defects in mandibulo facial dysostosis which suggests interference with the development of *structures arising from the first* and second branchial arches at an early stage This is probably due to disturbances in the migration of neural crest cells into the upper branchial arches (POSWILLO 1975 a) The middle ear cavity and its contents are formed by encroachment of the endoderm of the pharyngotympanic recess of the first arch The *ossicles arise from* condensations of connective tissue of the *first and* second arches which are initially adjacent to the *expanding tympanic* tube but eventually become incorporated This expansion continues after birth to form the mastoid antrum and air cells

It is this aspect of ear development that is most constantly affected in mandibulo-facial dysostosis It would seem that full expansion and *development* of the middle ear cleft does not occur The *differentiation* of the middle ear structures is disturbed and in particular the ossicles tend to *be fused* to each other or to the walls of the cavity It is difficult to decide from the tomograms or indeed at surgery what is a fused ossicle and what is a bony bar in the middle ear cavity

Con lusions Because of their distinctive appearance these children are diagnosed b-1 g d af at an early age and with hearing aids and suitabl- h lp can usually anage in a normal school However the moderately severe bilateral conductive afress with normal cochlear function makes surgical correction of the sound nducting mechanism highly desirable Prospects for success range from good cases with only slight attic atresia and ossicular fixation to hopeless where there sever atresia no attic or ossicles and only a slit middle ear cleft (Fig 7) Multi rectioral tomography of a high standard and careful audiologic assessment at an rly age are therefore of the outmost importance

SUMMARY

Deformities of the external and middle ear with conductive deafness are common in andibulo facial dysostosis but cochlear function is nearly always normal Twelve patients th the typical appearance and characteristics of the lesion are described All had some gr-- of atresia of attic and antrum with absent or deformed ossicles but 4 had external iditory meatu es of normal calibre The characteristic tomographic appearances of the ir are described

ZUSAMMENFASSUNG

Deformi aten ces ausseren und mittleren Ohres bei Mittelohrschwerhorigkeit sind ge vohnlich bei Dysostosis mandibulo-facialis jedoch ist die kochleare Funktion beinahe stets ormal Zwolf Patienten mit dem typischen Bild und den Charakteristika der Missbildung erden beschrieben Alle hatten eine gewisse Atresie des Atticus und Antrum ohne oder mit eformierten Gehorknochelchen 4 hatten jedoch einen ausseren Gehorgang von normalem Kaliber Das charakteristische tomographische Bild des Ohres wird beschrieben

RÉSUMÉ

Les déformations de l oreille externe et de l oreille moyenne avec une surdité de trans mission sont fréquente dans la dysostose mandibulo faciale mais la fonctio n cochleaire st presque toujours normale Les auteurs présentent douze malades ayant l aspect typique t les caractéristiques de cette lésion Tous avaient un certain degre d atresie de l attique t de l'antre avec des ossel ts absents ou déformes mais quatre avaient un conduit auditif externe de cal bre normal Les auteurs décrivent l aspect tomographique caracteristique de oreille

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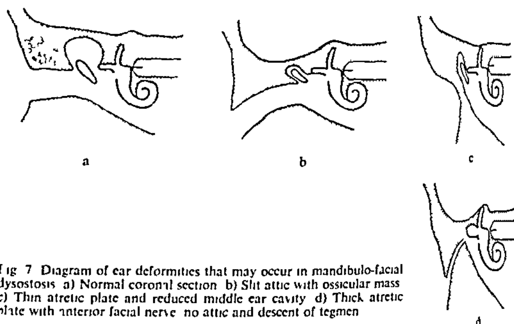


Fig 7 Diagram of ear deformities that may occur in mandibulo-facial dysostosis a) Normal coronal section b) Slit attic with ossicular mass c) Thin atretic plate and reduced middle ear cavity d) Thick atretic plate with anterior facial nerve no attic and descent of tegmen

Cochlear function is nearly always normal in these children and consequently the cochlea has a normal shape with a normal curl of the modiolus demonstrated by coronal tomography The only inner ear deformity in the present series involved the lateral semi circular canal In two cases this was shorter and wider than normal (Fig 7 d) This is the commonest inner ear anomaly demonstrated by tomography and has been described in mandibulo facial dysostosis by several authors (Sando et coll 1968 Phelps 1974 Hutchinson et coll) It is found also in craniofacial dysostosis thalidomide embryopathy anencephaly and chromosome trisomy abnormalities It may also be an incidental finding

There is a consistency of the defects in mandibulo facial dysostosis which suggests interference with the development of structures arising from the first and second branchial arches at an early stage This is probably due to disturbances in the migration of neural crest cells into the upper branchial arches (Poswillo 1975 a) The middle ear cavity and its contents are formed by encroachment of the endoderm of the pharyngotympanic recess of the first arch The ossicles arise from condensations of connective tissue of the first and second arches which are initially adjacent to the expanding tympanic tube but eventually become incorporated This expansion continues after birth to form the mastoid antrum and air cells

It is this aspect of ear development that is most constantly affected in mandibulo facial dysostosis It would seem that full expansion and development of the middle ear cleft does not occur The differentiation of the middle ear structures is disturbed and in particular the ossicles tend to be fused to each other or to the walls of the cavity It is difficult to decide from the tomograms or indeed at surgery what is a fused ossicle and what is a bony bar in the middle ear cavity

onclusions Because of their distinctive appearance these children are diagnosed ...re d af at an early age and with hearing aids and suitabl help can usually nage in a normal school However the moderately severe bilateral conductive fness with normal cochlear function makes surgical correction of the sound iducting mechanism highly desirable Prospects for success range from good cases with only slight attic atresia and ossicular fixation to hopeless where there vere atresia no attic or ossicles and only a slit middle ear cleft (Fig 7) Multi ectional tomography of a high standard and careful audiologic assessment at an ly age are therefore of the outmost importance

SUMMARY

Deformities of the external and middle ear with conductive deafness are common in *ndibulo-fa ial dysostosis* but cochlear function is nearly always normal Twelve patients th the typical appearance and characteristics of the lesion are described All had some gree of atresia of attic and antrum with absent or deformed ossicles but 4 had external ditory meatu es of normal calibre The characteristic tomographic appearances of the r are described

ZUSAMMENFASSUNG

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RESUME

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SPONDYLOMETAEPIPHYSEAL DYSPLASIA IN A MOTHER AND HER CHILD

H PETTERSSON and K O NILSSON

Spondylometaepiphyseal dysplasia is a term used to designate different types of ongenital osteochondrodysplasia in which significant abnormalities occur in the netaphyses and epiphyses of the tubular bones as well as in the spine (KOZLOWSKI 976) Pseudoachondroplasia first distinguished by MAROTEAUX & LAMY (1959) is he most common and best defined disorder but several other varieties of spondylo netaepiphyseal dysplasia have been reported (KOZLOWSKI 1974 1976 HESELSON et oll 1977)

This report concerns a newborn girl and her mother with abnormalities qualifying for the diagnosis of spondylometaepiphyseal dysplasia Different stages in the course of the dysplasia were reviewed retrospectively in the mother and at follow up of the daughter

The child The girl was born after a 39 week normal pregnancy Delivery was normal Birth weight 3 560 g CH length 47 cm Apgar score at one minute was 9 She had dis proportionately short arms and legs and was therefore admitted to the pediatric clinic where she has since been followed up for 5 years

No feeding problems always healthy except for ordinary children s diseases but retarded growth CH length was 60 cm at 6 months 62 5 cm at one year 70 cm at 2 years 76 cm at 3 years 82 cm at 4 years and 85 cm at 5 years She began to walk at 12 5 months of age but developed genu varum and a waddling gait Mobility of all

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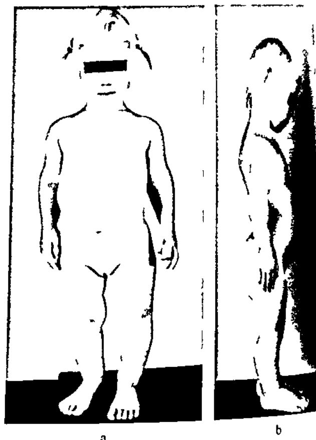


Fig 1 The child at 5 years of age Short arms and legs Accentuated lumbar lordosis and protruding abdomen

joints normal and no neurologic changes At one year of age palpation suggested rosary on the ribs and double malleols Treatment with vitamin D for 2 years had no effect on growth or skeletal development At about 2 years the lumbar lordosis was more accentuated than normally with protuding abdomen and has since remained so (Fig 1) Mental development has been normal

Blood count routine chemical examination of blood and urine determination of calcium and phosphor urinalysis for metabolic disorders including mucopolysaccharidosis as well as growth hormone and somatomedin assays revealed nothing abnormal The female karyotype was normal

Radiologic findings The wrists and ankles were examined every year A skeletal survey was performed at 2 days of age at 11 months (skull excluded) 18 months (skull and spine excluded) and at 5 years of age The findings may be summarized as follows

Skull 2 days Minute ossicles in relatively wide calvarial sutures 5 years Nothing abnormal

Spine 2 days Anterior arch of atlas not ossified A 2 mm ossific center of the odontoid process situated below the atlas (Fig 2 a) Ossified parts of vertebral bodies small and widely spaced on the cervical and lumbar regions Two coronal clefts in body of L4 one in L3 and one in L5 bodies 11 months Slight thoracic platyspondyli



a b

Fig. 2. Cervical spine of the child Lateral view a) at 2 days b) at 5 years of age At 2 days of age no ossification of the anterior arch of the atlas A 2 mm ossific center of the odontoid process located below the atlas (→) At 5 years of age short and pointed odontoid process Moderate cervical platyspondylia

Wedge shaped S1 body with pointed posterior margin (Fig 3) 5 years Short and pointed odontoid process (Fig 2 b) Moderate cervical and thoracic platyspondylia Concave irregular cranial surface of the lower thoracic vertebral bodies (Fig 4) Short posterior part of the S1 body accentuating lumbo sacral lordosis

Chest 2 days and 11 months Wide and cupped anterior osseous ends of the ribs 5 years Still wide costal ends but reduced cupping

Pelvis 2 days Small iliac wings Pubic bones ossified only in a small lateral part Distinctly outlined pointed rim of acetabular part of each iliac bone (Fig 5a) 11 months 18 months and 5 years Iliac wings remained small Acetabular rim still pointed at 11 months (Fig 5 b) but not later Ossification of pubic bone occurring on either side from a lateral and a medial center (Fig 5 b) which eventually fused (Fig 5 c) Irregular acetabular roof (Fig 5 c)

Tubular bones diaphyses 2 days 11 months 18 months and 5 years Marked shortness of all long tubular bones predominantly mesomelic and most marked in the radius Slight varus curvature of the femur and radius (Fig 6)

Tubular bones metaphyses (Figs 6 7) 2 days Broad metaphyses of all long tubular bones Pointed metaphyseal periphery in most long tubular bones (Fig 6 a c) and in



Fig 3 Lower lumbar and sacral spine of the child at 11 months of age Wedge shaped S1 body with pointed posterior margin

Fig 4 Lower thoracic spine of the child at 5 years of age Slight platyspondylia Concave irregular cranial surface of the lower thoracic vertebrae

Fig 3 Fig 4

some metacarpals 11 months to 5 years The pointed appearance of the periphery of the metaphyses gradually vanished during the first 2 years of life The metaphyses of long tubular bones remained broad and had an irregular but distinctly defined surface along the epiphyseal cartilage Normal distance between epiphyseal ossification center and metaphysis Several small irregular ossification centers developed outside the medial margin of some metaphyses but were slowly incorporated into the metaphysis which thereby became still broader (Fig 7 b c) Short and broad femoral neck

Tubular bones epiphyses (Figs 5 6 7) 2 days Epiphyseal ossification center visible only in distal femur (Fig 7 a) 11 months to 5 years Slow and at some sites multicentric epiphyseal ossification of long tubular bones much more marked in the femoral head than elsewhere (Fig 5 c)

The mother Height only 147 cm and arms and legs short She had been radiologically examined at 4 5 years of age because of supposed rickets and was re examined after the birth of the daughter she was then 30

Born at term delivery normal CH length at birth 46 5 cm body weight 3 130 g head circumference 35 cm Observed in hospital for first 6 weeks of life because two years earlier her mother had been treated for pulmonary tuberculosis She then seemed to develop normally and routine blood and urine examinations revealed nothing abnormal Later growth was retarded From 2 to 5 years of age she was treated for assumed rickets because of genu varum Harrison s groove and a suggested rachitic rosary No history of any other disease during childhood

Radiologic findings 4 5 years of age (knees wrists chest including thoracic spine) Slight thoracic platyspondylia with a shape of the vertebral bodies resembling

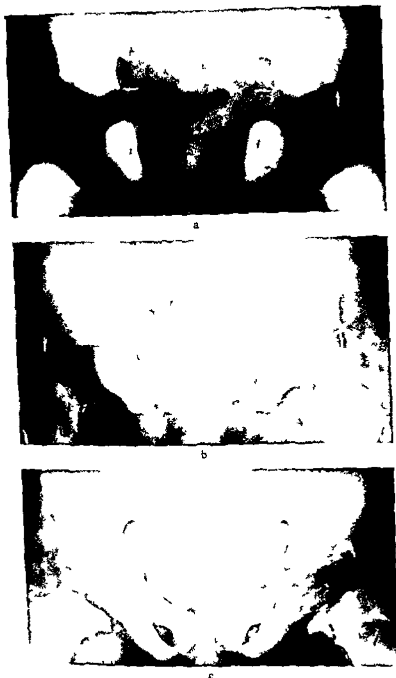


Fig. 5 Pelvis and hip joints of the child a) at 2 days of age b) at 11 months c) at 5 years of age Pointed acetabular rim (→) at 2 days and 11 months of age Slow ossification of the pubic bones [illegible] at acetabular roof Multicentric ossification of the femoral heads



Fig 3 Lower lumbar and sacral spine of the child at 11 months of age Wedge shaped S1 body with pointed posterior margin

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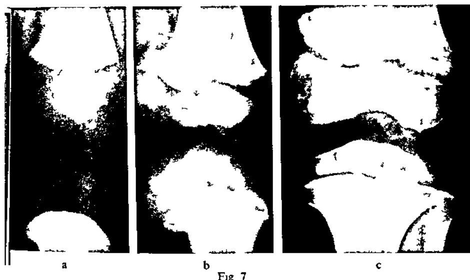


Fig 7



Fig 7 Left knee of the child a) at 2 days b) at 18 months c) at 5 years of age Broad metaphyses with irregular but distinctly defined surface towards the epiphyseal cartilage Irregular ossification center outside the medial margin of the femoral metaphysis (b) fused with the rest of the meta physis at 5 years of age (c)

Fig 8 The mother Left knee at 4 5 years of age The same appearances as in the girl at 5 years of age (cf Fig 7c)

Fig 8

Family history

The parents of the girl were not related The girl had only one sibling a sister She was of normal length with normal body proportions and appeared healthy Radiography of the sister at 8 years of age (skull thoracic spine pelvis long bones) revealed nothing abnormal

The only sibling of the mother a sister was stillborn death following intrauterine asphyxia after a normal pregnancy Autopsy revealed no further abnormality



Fig 6 Left arm and leg of the child a c) at 2 days of age b d) at 5 years of age Mesomelic shortness of the long bones especially affecting the radius Pointed metaphyseal periphery of most long bones at 2 days of age (→) Broad metaphyses with irregular but distinctly defined surface towards the epiphysis at 5 years of age Normal thickness of the epiphyseal cartilage (b d)

that in the girl Somewhat broad and cupped anterior osseous ends of the ribs Broad irregular metaphyses of the knees and wrists as in the girl but less evident (Fig 8 Irregular distal epiphyses of femur and radius

30 years of age (total skeletal survey) Spine Hypoplastic odontoid process (Fig 9 Slight cervical and thoracic platyspondylia with irregular end plates (Figs 9 10 Short posterior part of S1 body

Pelvis Small iliac wings Sloping and shallow acetabular roofs

Long bones Short diaphyses with broad proximal and distal ends Short femoral neck Slightly bowed radius

Hands Hypoplastic and sclerotic proximal part of scaphoid

coll 1974) The most conspicuous osseous abnormalities at birth were those of the metaphyses which in the girl initially had a strikingly pointed periphery A similar appearance has been observed in several severe forms of dysplasia e g achondrogenesis type I tanatophoric dwarfism the Saldino Noonan type of the short rib-polydactylia syndrome and in less severe conditions as the Schmid type of metaphyseal dysplasia (SPRANGER et coll 1974) as well as in achondroplasia (CREMIN & BEIGHTON 1978) However in the girl these conditions could be excluded already neonatally either on the basis of absence of characteristic components of the respective syndromes or concomitant abnormalities of the epiphyses and the spine

In spondylometaphyseal dysplasia the spinal abnormalities appear to have included absence or non ossification of the odontoid process in only 2 cases on record (FELMAN 1974) The epiphyses were normal in both of them as in any other established type of this dysplasia

The spondylometaepiphyseal dysplasia group of syndromes seems to be the only category in which any of the osseous abnormalities in the present cases may occur but no type of spondylometaepiphyseal dysplasia has been shown to comprise all abnormalities demonstrated The early onset at least in the girl the nearly normal hands and the absence of protruding anterior parts of vertebral bodies differ from the findings described in the original report on pseudoachondroplasia (MAROTEAUX & LAMY 1959) as well as from those in the four types distinguished later by MALONEY (1969) HALL & GROSSMAN (1969) WADIA (1969) HALL & DORST (1969) and in the series recently reported by HESELSON et coll (1977) The normal appearance of the skull and the absence of scoliosis and of hypoplastic vertebral bodies seem inconsistent also with the micromelic type of spondylometaepiphyseal dysplasia described by KOZLOWSKI (1974) The findings further exclude the condition originally referred to by KOZLOWSKI & BUDZINSKA (1966) as combined metaphyseal and epiphyseal dysostosis and later by KOZLOWSKI (1976) considered as a form of spondylometaepiphyseal dysplasia

The syndrome common to the present two cases thus appears to be a previously not described type of spondylometaepiphyseal dysplasia Special features of this type include a slowly ossifying and hypoplastic odontoid process of the epistropheus a short dorsal aspect of the S1 body small iliac wings broad and cupped anterior osseous margins of the ribs and in infancy a conspicuous pointed periphery of the metaphyses The last mentioned feature is of particular interest because several other forms of dysplasia with a similar shape of the metaphyses are fatal neonatally or in infancy It is evident from the follow up of the girl that this finding is not necessarily a sign of a bad prognosis and that it will not even permit prediction of local development In this case the neonatal deformity of the metaphyses was followed by further abnormality at some sites but in the hands for example subsequent growth seemed to be almost unaffected

It is noteworthy that although the radiologic findings in the present cases were definitely abnormal at all ages the deviations from normal markedly changed in



Fig 9



Fig 10

Fig 9 Cervical spine of the mother at 30 years of age Hypoplastic odontoid process Slight platyspondylia

Fig 10 Thoracic spine of the mother at 30 years of age Slight platyspondylia Irregular end plates

The maternal grandmother had no history of disease except for the tuberculosis already mentioned Her height was 160 cm with normal body proportions Radiography of the chest at 31 years of age revealed normal ribs thoracic vertebrae and shoulders Examination of the wrists at the age of 61 years demonstrated a fracture of the radius but no further abnormality

The maternal grandfater was 185 cm high and had no history of disease

The father of the girl was 159 cm high Radiography at the age of 32 (total skeletal survey) revealed no abnormalities Most members of his family were said to have been rather small for many generations but not physically disproportional

Discussion

The treatment of the girl and her mother for assumed rickets was prompted by rather ambiguous clinical findings This diagnosis was not supported by radiologic or laboratory observations and became untenable with the course of the disease

The similarity between the findings made in the mother and her daughter at the age of 4 5 and 5 years respectively strongly suggests some hereditary congenital dysplasia causing shortness of stature The family history makes a dominant inheritance probable

The laboratory tests excluded metabolic disorders such as mucopolysaccharidosis and mucolipidosis and the radiologic findings are inconsistent with achondroplasia as well as with diastrophic metatrophic and parastremmatic dwarfism (SPRANGER

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NADIA R Four types of pseudoachondroplastic spondyloepiphyseal dysplasia (SED) F 3 — Dominant Maroteaux Lamy type in three generations of whom three affected persons are described here Birth Defects Original Article Series 5 (1969) 250

appearance as skeletal growth proceeded The findings made in the mother at the tim of the birth of her daughter are so dissimilar to those in the newborn baby that, with out knowledge of the familial relationship they would probably not have been attributed to one and the same syndrome in both Even despite this knowledge they might have been thought to reflect different diseases if both patients had not been examined also at similar ages Since in spondylometaepiphyseal dysplasia as in m ny other congenital dysplasias some diagnostic features will disappear or become less characteristic in the course of the disease observations within the optimum range of age may be essential to avoid erroneous classification Age differences may be very misleading in attempts to distinguish and define various types of a syndrome

Despite the obvious similarities between the findings made at 4 5 to 5 years of age in the present cases these examinations also revealed some differences in the mani festation of the dysplasia These variant types might be attributed to different ex pressivity of the abnormal genotype underlying the syndrome It appears likely that the clinical course will be somewhat less favourable in the daughter than it has been in her mother

SUMMARY

Variant types of spondylometaepiphyseal dysplasia in a mother and her child is reported Several stages of the disorder are presented demonstrating the principal difficulties in dis tinguishing variant types of skeletal dysplasia

ZUSAMMENFASSUNG

Verschiedene Typen von spondylometaepiphysealer Dysplasie bei einer Mutter und ihrem Kind werden beschrieben Mehrere Stadien der Erkrankung werden beschrieben welche zeigen dass prinzipielle Schwierigkeiten in der Unterscheidung verschiedener Typen von Skelettdysplasie vorliegen

RÉSUME

Les auteurs rapportent des variantes de la dysplasie spondylo métaépiphysaire chez une mére et son enfant Ils présentent différents stades de la maladie mettant en évidence le principales difficultés pour distinguer les variantes de la dysplasie squelettique

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Table

Review of 8 cases with vesicoureteric reflux grade III and urinary tract infection The diagnosis is based on the presence of >100 000 bacteria/ml voided urine The infection is classified as pyelonephritis (P) when at least 2 of the following criteria were fulfilled fever abdominal pain or increased ESR

Case No	Age (years) during observation period	Age (years) at infection		Relative size (per cent) at	
		Before observation	During observation	First urography	Last urography
1	03 55	02 P	25 P 28 37 P	90	74
	10-45	06 P 08	20 P 25 35 P 40	71	66
3	13 51	10 P 12 P	23 P 26 P	118	91
4	15-45	05 P 09 P 11	15 P	101	84
5	35 80	35 P	40 55 75 P	7?	51
6	55 117	35 P 55 P	58 P 75 P 95 P 110 P	67	44
7	65 105	40 P	No	80	84
8	85 13?	30 P 80 P	105 120 130	94	77

All patients were treated immediately following the onset of symptoms A urine culture was obtained before treatment In cases where the bacteria proved to be resistant to the antibiotic first chosen the antibacterial therapy was changed In all patients urine cultures were obtained every second month during the entire time of observation Each episode of asymptomatic bacteriuria was treated with the proper antibacterial therapy The treatment lasted for 10 days In addition all patients were given prophylactic treatment with nitrofurantoin for varying periods ranging from 1 to 24 months

The following classification of reflux was used Grade I reflux into the ureter not reaching the pelvis Grade II reflux with complete filling of the upper urinary tract

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VESICOURETERIC REFLUX AND PYELONEPHRITIS

Long time effect on area of renal parenchyma

I. WIKSTAD, A. APERIA, O. BROBERGER and K. EKENGREN

In children with urinary tract infection, scarring of the kidney parenchyma (SCOTT & STANSFELD 1968, ROLLESTON et coll. 1970, SHAH et coll. 1978) and reduced renal function (APERIA et coll. 1976) generally imply either that reflux from the bladder reaches the kidney pelvis or that the urinary outflow is obstructed. A causative relationship between vesicoureteric reflux in combination with urinary tract infection and renal parenchymal injury is, however, not proved by the findings of a common incidence. One examination of the urinary tract cannot exclude the possibility that a fulminant cystopyelitis in early infancy will result in an injury to the parenchyma or in a vesicoureteric reflux or both.

The relative growth of kidneys with vesicoureteric reflux has been followed in 8 children at repeat examinations during 3 to 6 years and the results are now reported.

Material

The series consisted of 8 girls ranging in age from 4 months to 13 years. The height and weight of all patients were within ±2 SD of normal mean of Swedish girls. All patients had recurrent urinary tract infection with fever, abdominal pain or increased ESR and vesicoureteric reflux grade III. In cases with bilateral reflux, the kidney with the most extensive pyelonephritic scarring was included in the retrospective analysis. A summary of the histories of the urinary tract infections is given in the Table.

Submitted for publication 14 October 1977.



Fig 2 Micturition cystography Pelvis and ureter are most dilated at end of micturition (cf Fig 1)

itial examination were excluded because the rapid phase of reduction had probably lready passed

All patients admitted to the nephrology section of this pediatric clinic during ?0 to 1977 fulfilling the criteria mentioned were included in the series

None of the patients was subjected to operation during the observation period i the youngest patients it was hoped that the vesicoureteric reflux would heal spon aneously In other cases the parents did not want an operation

Methods

Urography was performed with the standard technique using a film focus distance f 100 cm Contrast medium (Urografin 60 %) was injected intravenously in a dose f 0 5 to 2 ml/kg body weight The size of the renal parenchymal area was determined planimetrically The details of this method have been previously described (APERIA et coll 1978) The area was referred to 1 73 m² body surface Micturition cystography was carried out following infusion of contrast medium into the bladder at low pres sure the film focus distance was 100 cm

Results

Two examinations with an interval of 4 years in a representative case is illustrated in Fig 3 The patient had reflux grade III on the right side At the initial urography at the age of 5 years the size of the right kidney was 67 per cent of that expected for

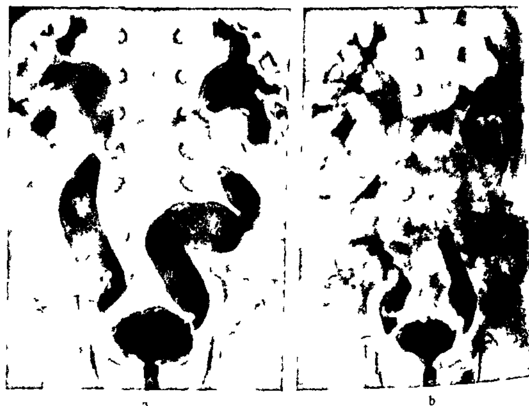


Fig 1 Micturition cystography Pelvis and ureter most dilated at beginning of micturition (b)

without dilatation Grade III reflux with complete filling of the upper urinary tract and dilatation of the ureter or of both the ureter and the pelvis The dilatation of the ureter and the pelvis in grade III may vary at the same examination (Figs 1 2). As only one exposure was usually made to demonstrate the reflux it is impossible to ascertain whether the exposure was made at the time of maximum dilatation There fore no further sub classification of reflux grade III was made on the basis of the degree of dilatation No intrarenal reflux was observed in the present series On the contralateral side the kidney pelvis and ureter were normal in 3 cases reflux grad II was recorded in 3 and grade III in 2 cases

The following criteria were used for inclusion of a patient in the series At least 2 urographies should have been performed and the interval between the initial and the last one should exceed 26 months Reflux grade III should have been demon strated at repeat examination No patient with duplicated urinary tracts was a cepted and no operation in order to correct reflux should have been performed

The experience indicates that in vesicoureteric reflux and pyelonephritis the reduc tion of the renal parenchyma will proceed until the size of the kidney will be ap proximately 50 per cent of the size expected for the age After that the relative size of the kidney seems to be unaltered at least until the child reaches puberty There fore all patients with reduction of the relative size with 50 per cent or more at the

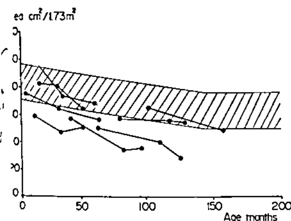


Fig 4 Relative size of kidney with vesicoureteric reflux grade III during observation of 3 to 6 years A line connects individual observations on the same kidney at different times The shaded area indicates the normal size of a kidney within ±2 SD limits

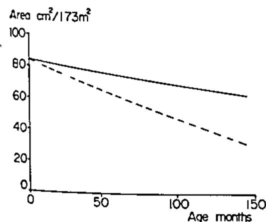


Fig 5 Solid line illustrates decrease of kidneys during the first 12 years of life and broken line decrease of relative size of kidneys with vesicoureteric reflux grade III The lines are adjusted to start at the same point The angle between the 2 lines is significantly different from zero

The alteration of the outline of the kidney parenchyma from the initial to the last urography is illustrated in Fig 6 Obvious scarring appeared in one or both poles of the kidney in 5 patients and laterally in one patient In 2 of the 8 patients the relative decrease in the size of the parenchyma might be due to growth retardation without obvious focal scarring

In 3 cases (Nos 4 5 7) no vesicouteteric reflux existed on the contralateral side and a continuous compensatory growth of the kidney occurred (Fig 7)

Discussion

Vesicoureteric reflux grade III when associated with urinary tract infection will result in a progressive decrease in size of the renal parenchyma in relation to the size of the individual The relative importance of the 2 factors i e vesicoureteric reflux and urinary tract infection for the injury to the kidney remains unclear As previously reported bacteriuria appears to have no effect on the renal function provided

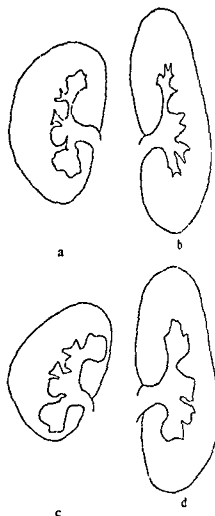


Fig 3 Girl with reflux grade III on the right side a) First examination Right kidney is small (67 of normal size) with reduced parenchyma b) Right kidney compensatorily enlarged (121 of normal size) c d) Four years later c) Right kidney is smaller than previously due to progressive scarring (58 of normal size) d) Compensatory hypertrophy of left kidney has increased (129 of normal size)

the age The size of the contralateral kidney was 121 per cent of the expected Four years later the right kidney had decreased to 58 per cent of the expected and the contralateral kidney increased to 129 per cent

The decrease in the renal parenchymal areas in the 8 patients with reflux grade III is demonstrated in Fig 4 At the initial urography the size of the kidneys ranged from 67 to 118 per cent of that expected for the age and at the last one from 54 to 91 per cent of the expected size During the first 12 years of life the area of normal kidneys determined planimetrically decreases with 0 15 cm²/month in relation to the area of the body (Aperia et coll 1977) The relative size of kidneys with vesicoureteric reflux grade III included in the present series decreased with 0 34 cm /month during this period of life (Fig 5)

The ratio by which the relative size of the kidney decreased was well correlated (r = 0 65) to the numbers of episodes of pyelonephritis and somewhat less to the total number of urinary tract infections However the correlation between the absolute size of the kidney and the number of attacks of pyelonephritis as well as the number of urinary tract infections was slightly lower

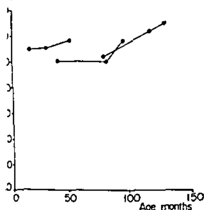


Fig 7 Development of compensatory growth in the 3 patients who had kidneys with normal ureters and a contralateral kidney with vesicoureteric reflux grade III A line connects measurements made on the same kidney

flux All these observations further support the hypothesis that usually only cases ith reflux reaching the renal pelvis will develop pyelonephritis which together with te vesicoureteric reflux per se will result in injury to the parenchyma

At the time of the initial examination 4 of the kidneys with reflux grade III were of ormal size as expected for age or larger Yet at the second examination the relative ize of these kidneys had decreased at a rate faster than normal Thus the initial size f the kidney will not predict the risks for injury to the kidney in cases with persistent esicoureteric reflux grade III associated with repeat episodes of pyelonephritis Therefore urinary tracts with vesicoureteric reflux grade III which for one reason or another are not operated upon must be observed with repeat urographies

Acknowledgement

The authors are indebted to Nils Wikstad for statistical advice Financial support was received from the Swedish Medical Research Council (B77 19X 2049 11) and the fund of Karolinska Institutet Stockholm

SUMMARY

The effect of gross vesicoureteric reflux in combination with urinary tract infection on the area of the renal parenchyma was analysed in 8 non selected girls during 3 to 6 years A progressive significant decrease of the relative size of the kidneys with vesicoureteric reflux occurred as compared with that of kidneys with normal ureters The decrease was mainly due to scars in the upper and lower poles A positive correlation was found between the reduction of parenchyma and the number of episodes of pyelonephritis

ZUSAMMENFASSUNG

Der Effekt eines bedeutenden vesico-uretären Refluxes in Kombination mit einer Infektion der Harnwege auf die Fläche des Nierenparenchyms wurde bei 8 nicht-selektierten Madchen während 3 bis 6 Jahre festgestellt Eine progressive signifikante Verminderung der relativen

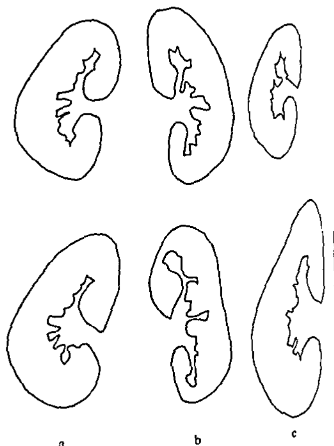


Fig 6 a) Case 4 General growth retardation Top Area of renal parenchyma at first examination is 101 of normal size (21 cm²) Bottom 3 years later The area is 84 of normal size (24 cm²) b) Case 5 Parenchymal scarring Top Small kidney without evident scarring at first examination (20 cm² 72 of normal size) Bottom 4 5 years later Parenchymal scarring in both poles with alteration of calices The area has diminished to 51 of normal size (19 cm²) c) Case 1 General growth retardation less evident without measurement Top Area of renal parenchyma at first examination is 90 of normal size (14 cm²) Bottom 5 years later Area is 28 cm² which is a relative decrease to 74 of normal size

no or only a slight reflux is present that does not reach the renal pelvis (APERIA et coll 1976) The importance of pyelonephritis for renal parenchymal injury to urinary tracts with reflux grade III is suggested by the positive correlation between the number of pyelonephritic episodes and the rate by which the relative size of the kidney decreased However it is noteworthy that proper medical treatment of the urinary tract infection did not prevent the injury to the renal parenchyma The present results do not allow any evaluation of the effect of vesicoureteric reflux as such on the function of the parenchyma Only experiments have offered some evidence that refluxes also in cases with sterile urine result in renal injury (HELIN et coll 1975 HODSON et coll 1975 MOFFAT & LAURENCE 1976 MORGAN et coll 1976)

The relative decrease in the size of the renal parenchyma appears in most cases to be due to scarring rather than to growth retardation This observation is in accordance with that made by ROLLESTON et coll (1974) who in children with gross vesicoureteric and intrarenal reflux found focal parenchymal lesions at the site of the intrarenal reflux Progression of renal injury has been observed in 73 per cent of kidneys with reflux grade III but only in 20 to 25 per cent of kidneys with reflux grade I and II (FILLY et coll 1974) HODSON (1964) reported that 80 per cent of the scarred kidneys in young children had severe vesicoureteric reflux and SHAH et coll that 98 per cent of kidneys with radiologically demonstrable scars were drained by ureters with

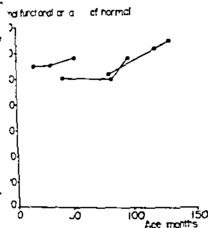


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Der Effekt eines bedeutenden vesico-uretären Refluxes in Kombination mit einer Infektion der Harnwege auf die Fläche des Nierenparenchyms wurde bei 8 nicht-selektierten Mädchen während 3 bis 6 Jahre festgestellt Eine progressive signifikante Verminderung der relativen

Grosse der Nieren mit vescio uretarem Reflux trat auf verglichen mit Nieren mit normalen Uretiten Die Verminderung war hauptsachlich die Folge von Narben in den oberen und unteren Polen Eine positive Korrelation zwischen der Verminderung des Parenchyms und die Anzahl von Schuben von Pyelonephritis wurde gefunden

RESUMÉ

Les auteurs ont étudié pendant 3 à 6 ans sur 8 fillettes non sélectionnées l effet sur le parenchyme rénal du reflux vésicourétéral important associé avec une infection des voies urinaires Ils ont constaté une diminution progressive importante de la taille relative des reins en rapport avec le reflux vésicourétéral par comparaison avec la taille des reins qui avaient des uretères normaux La diminution de taille a été due surtout à des cicatrices dans les pôles supérieurs et inférieurs Les auteurs ont trouvé une corrélation positive entre la réduction du parenchyme et le nombre des épisodes de pyélonéphrite

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MASSIVE CONGENITAL TRICUSPID INSUFFICIENCY IN THE NEWBORN

H G BOGREN R IKEDA T A RIEMENSCHNEIDER D F MERTEN
and G G JANOS

In 1866 EBSTEIN described autopsy findings from a case of tricuspid insufficiency with dysplasia and displacement of the tricuspid valve Since then more than 300 cases of so called Ebstein s anomaly have been described (GENTON & BLOUNT 1967) In recent years dysplasia of the tricuspid valve without displacement of any leaflet has been recognized as a separate entity (BECKER et coll 1971) although described earlier (BARRITT & URICH 1956) Other types of congenital tricuspid incompetence are those in combination with pulmonary atresia with intact ventricular septum (DAVIGNON et coll 1961 BARR et coll 1974) or corrected transposition of the great vessels (with Ebstein s malformation of the left atrioventricular valve DEKKER et coll 1965 BECKER et coll 1971)

The clinical diagnosis of massive congenital tricuspid insufficiency is important as spontaneous improvement and resolution has been reported (BOUCEK et coll 1976) Three cases of massive congenital tricuspid insufficiency are now presented from diagnostic pathologic and etiologic points of view

Case reports

Case 1 Male infant (3 000 g) born after 42 weeks gestation at spontaneous delivery Apgar score was 5-6 at birth somewhat improving after suctioning and oxygen stimulation Physical examination Central cyanosis and respiratory distress were noted A grade 3/6 systolic ejection murmur was heard over the precordium ECG Evidence of right axis

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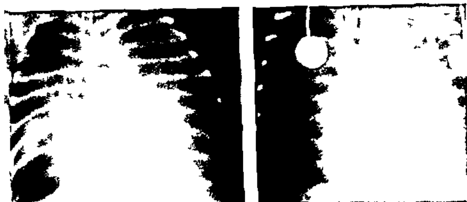
Fig 1 Case 1 Massive cardiomegaly with severe right atrial and right ventricular enlargement and decreased pulmonary vascularity A pneumomediastinum is present An ECG wire and a chest tube are superimposed on the lateral view



Fig 2 Case 2 Cardiomegaly with massive right atrial and right ventricular enlargement and markedly decreased pulmonary vascularity An umbilical artery catheter is superimposed on both views

deviation right atrial enlargement and right ventricular hypertrophy The infant was hypoglycemic and responded well to therapy with 25% glucose Clinical impression Cyanosis due to valvular pulmonic stenosis and atrial septal defect or patent foramen ovale

Case 2 Female infant (2 800 g) born at term after pitocin induced labor Mother had pre-eclampsia with hypertension The infant was asphyxiated at birth and had an Apgar score of 2 at one min and five min of age and was immediately intubated and placed on a respirator Physical examination Flaccid edematous unresponsive infant with severe cyanosis despite intubation and 100% oxygen respiration The heart sounds were muffled A grade 3/6 holosystolic murmur was heard over the left and right lower sternal borders and a grade 2/6 diastolic murmur was heard over the third left intercostal space A systolic lift was



ig 3 Case 3 Extreme cardiomegaly due to greatly enlarged right atrium and right ventricle De
-eased pulmonary vascularity

isible and palpable at the left lower and right upper sternal borders ECG Evidence of ight axis deviation slurred rR complexes across the precordium The infant was treated ith digitalis and dieuretics without improvement Clinical impression Cyanosis congestive eart failure due to tricuspid insufficiency and probably Ebstein s malformation

Case 3 Premature female infant (2 100 g) Mother had influenza like illness during the econd month of pregnancy The infant was flaccid at birth severely cyanotic with an Apgar score of 1–2 She was intubated in the delivery room resuscitated and placed in a espirator Physical examination Central cyanosis on respirator with 100 % oxygen The heart sounds were distal and a grade 3/6 systolic murmur was heard over the left lower sternal border A prominent thrill and lift was palpable at the lower left sternal border Congestive heart failure and hepatomegaly were present ECG Evidence of right axis deviation right atrial enlargement and right ventricular preponderance Clinical impression Cyanosis and congestive heart failure due to severe tricuspid insufficiency secondary to tricuspid valve dysplasia or Ebstein s anomaly

Radiography of the chest

All 3 cases had massive cardiomegaly with greatly enlarged right atria and enlarged ight ventricles (Figs 1–3) The massively enlarged rounded right atrium forming he right heart border is particularly impressive in all cases and is diagnostic of evere tricuspid insufficiency The markedly enlarged right ventricles impinge on he retrosternal space form the left heart borders and displace the left ventricle posteriorly (Fig 7) The right atrium is by far the largest chamber of the heart in all cases and fills up most of the chest in Case 3 It is so large that it even forms the posterior heart border in all cases who also have markedly decreased pulmonary vascularity The detailed right heart anatomy demonstrated at cardioangiography is illustrated in Figs 4 to 6 Case 1 also had a pneumomediastinum There was no evidence of left atrial or ventricular enlargement (Fig 7)

Cardiac catheterization

The data on catheterization appear in the Table A venous catheter could be advanced in normal fashion into the right atrium and the right ventricle but it could



Fig 4 Case 1 Frames from p a and lateral right ventricular cineangiography Massive tri ... d regurgitation without evidence of tricuspid valve displacement Faint filling of the pulmonary artery The right atrium is huge and forms the posterior heart border

not be advanced into the pulmonary artery in any of the 3 cases In all cases th catheter passed through a foramen ovale or atrial septal defect into the left atrium and in 2 cases to the left ventricle The oxygen saturations were decreased in th left atrium and the left ventricle in all cases indicating a marked right to left shunt at the atrial level All cases had elevated right atrial pressures which were equal to or higher than the left atrial pressures All 3 infants had elevated right ventricular end diastolic pressures and Case 2 had elevated left ventricular end diastolic pressure consistent with congestive heart failure Case 1 had systemic right ventricular systolic pressure the others had normal or moderately elevated right ventricular systol pressures for the immediate newborn period This was probably due to a very poor forward flow from the right ventricle into the pulmonary artery The pulmonary artery could not be entered in any patient The pulmonary artery pressures were presumably approximately equal to the right ventricular pressures and not particu larly high in Cases 2 and 3 This again was probably due to the poor flow in the pulmonary circulation The pulmonary vascular resistance could not be evaluated but was presumably high as the pulmonary flow is inversely related to the pulmonary resistance All pressure and oxygen saturation measurements obtained are given in the Table

Cardioangiography

One to two ml Renografin 76 % per kg body weight were injected into the right ventricle in all 3 cases and biplane cineangiography with cesium iodide image intensification 64 frames per second was performed Large amounts of contrast medium flowed from enlarged right ventricles into greatly enlarged right atria indicating severe tricuspid valvular insufficiency using previously described criteria (Bogren et coll 1972) The right atria and ventricles all had very poor contractility and contrast medium regurgitated back and forth between them for several minutes



Fig 5 Case 2 Frame from p a right ventricular cineangiography Massive tricuspid regurgitation without evidence of tricuspid valve displacement Huge right atrium



a



b

Fig. 6 Case 3 Frames from p a and lateral right ventricular cineangiography Massive tricuspid incompetence without evidence of Ebstein s anomaly Massive enlargement of right atrium forming both lateral and posterior borders of the right side of the heart

Cine frames appear in Figs 4 to 6 It is evident that the right atrium is the largest cardiac chamber in all 3 cases it forms the right and posterior heart borders and at least in Case 3 is larger than the other cardiac chambers together The tricuspid valve appears to be situated in normal position and there is no evidence of displacement of the valve or atrialization of the right ventricle using the criteria described by Hipona & Arthachinta (1965) or Soloff et coll (1957) There was no evidence of pulmonic stenosis although the pulmonic valve was difficult to evaluate because of the massive tricuspid valve regurgitation which caused marked dilution of the contrast medium In Case 1 a right ventricular outflow tract injection was

Table

Data on cardiac catheterization

		Case 1	Case 2	Case 3
Descending aorta (umbilical artery catheter)	Pressure		61/30 $\overline{50}$	73/30 $\overline{45}$
	O_2 saturation		64	
Left ventricle	Pressure		65/11	68/9
	O_2 saturation			64
Left atrium	Pressure	a wave 13 v wave = 6 $\overline{6}$	a wave = 10 v wave = 6 $\overline{7}$	a wave 7 v wave 8,6
	O_2 saturation	84 *	64	55
Right atrium	Pressure	a wave = 13 v wave = 8 $\overline{6}$	a wave = 11 v wave = 10 $\overline{8}$	a wave 7 v wave 6 6
	O_2 saturation	66		
Right ventricle	Pressure	68/12	27/8	38 9
	O_2 saturation	62		
Left ventricular end diastolic pressure after cineangiography			$\overline{14}$	$\overline{12}$
Left atrium after cineangiography				$\overline{10}$
Right atrium after cineangiography				$\overline{15}$

made to demonstrate the pulmonic valve more in detail No definitive pulmonic stenosis was found The pulmonary arteries were hypoplastic in all cases and the flow from the right ventricle to the pulmonary circulation appeared markedly decreased

Left sided injections were also performed at which normal left hearts were found The ventricular septum was intact in all cases (Fig 7) The atrial septum was difficult to evaluate because of the marked dilution of the contrast medium at the right sided injections No right to left shunt at the atrial level could be seen with certainty (although suggested in Case 2) due to superimposition on the left atrium by contrast medium in the right atrium and ventricle and no left to right shunt was present as seen from left atrial injections The catheterization data however indicated a right to left shunt at the atrial level

A patent ductus arteriosus was found in all 3 cases with flow from the aorta into the pulmonary artery (Fig 7) In Case 3 there was also evidence of pulmonic valvular insufficiency with contrast medium flowing from the aorta into the pulmonary artery and in a retrograde fashion across the pulmonic valve into the right ventricle

The cardioangiographic and cardiac catheterization diagnosis was identical in all 3 cases massive tricuspid valvular insufficiency right to left shunt at the atrial level through a patent foramen ovale or atrial septal defect and left to right shunt through a patent ductus arteriosus In spite of the patent ductus arteriosus there appeared to



ig 7 Case 3 Frames from p a and lateral left ventricular cineangiography The left ventricle has normal size but is displaced posteriorly and does not form the left or posterior heart border Patent ductus arteriosus

be decreased flow through the pulmonary circulation due to hypoplastic pulmonary arteries

Clinical course

Case 1 was thought to have pulmonic stenosis because of the high right ventricular pressures and the decreased pulmonary vascularity Angiographically there was no positive evidenc of pulmonic stenosis but becaus of the dilution of contrast medium it was felt that pulmonic stenosis could not be excluded The patient did very poorly clinically and it was felt that the only thing that could save his life was to operate a pulmonic stenosis if there was one The patient was therefore operated upon but no pulmonic stenosis was found The patent ductus arteriosus was ligated but the infant did not survive the postoperative period The other 2 infants deterio rated rapidly and all 3 infants were dead within 34 hours

Autopsy findings

Case 1 measured 48 cm from crown to heel and the heart weighed 33 g Both the right atrium and right ventricle were dilated The striking finding was numerous large smooth warty excrescences of up to 3 mm in diameter coating the tricuspid valve leaflets primarily on the atrial surface These dysplastic changes (BECKER et coll 1971) extended on to the chordae in fused masses and thus obliterated the true free edges of the leaflets Most severely affected was the septal cusp which had large excrescences covering the atrial surface of the leaflet and extending on to the chordae tendineae The origins of all three leaflets were clearly from the annulus fibrosus between the right atrium and ventricle (Fig 8)

Case 2 measured 45 cm from crown to heel and the heart weighed 29 g The right atrium was strikingly enlarged and the right ventricle was obviously dilated Again

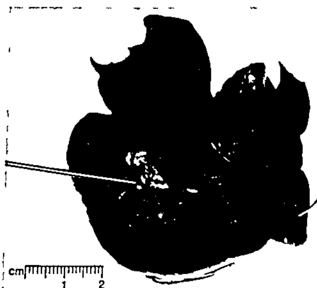


Fig 8 Case I Dysplastic changes of the tricuspid valve leaflets (wartlike excrescences) extending onto the chordae tendineae No fusion or adhesion to the underlying endocardium

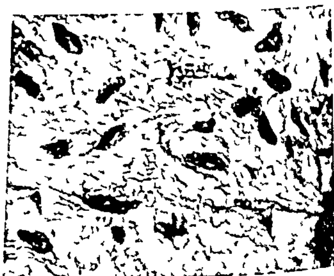


Fig 9 Case 1 Section of the dysplastic tricuspid valve Fibroblasts in connective tissue with no inflammatory reaction Magnification 350

smooth warty excrescences coated the tricuspid leaflets and chordae They were only up to 1 mm in diameter but again formed a fused sheet like dysplastic mass which covered the chordae The septal leaflet appeared to originate from the muscular part of the ventricular septum and not from the annulus fibrosus Both the anterior and posterior cusps arose from the fibrous ring The pulmonary valve cusps were also moderately thickened (0 5 mm) along the free edges

Case 3 measured 40 cm from crown to heel and the heart weighed 25 g The right atrium again was strikingly dilated The smooth excrescences were even smaller than in Case 2 Again they coated the atrial surface and the chordae as a thin warty sheet The leaflets seemed to have a normal origin but the septal leaflet was fused to the wall of the right ventricle on the side next to the posterior cusp In this case as in Case 2 the pulmonic valve cusps had thickened rounded free borders

Microscopically all the excrescences were loose edematous collagenous tissue ith a few scattered fibroblasts and no inflammatory cells (Fig 9) The lesions were l covered by an endocardial lining In Case 2 the septal cusp seemed to arise om the muscular septum and no obvious fusion of the inferior surface of the valve aflet with the muscular wall was proven

In summary all 3 cases grossly and microscopically had the classical dysplastic hanges as originally described by EBSTEIN and more recently summarized by ECKER et coll In addition one case had a mildly displaced cusp the so-called bstein s anomaly The excrescences in all cases were extensive and formed eet like masses that involved the chordae These changes grossly obliterated any ognizable free edge on any of the tricuspid leaflets With these gross changes mproper closure of the valve leaflets had led to insufficiency and dilatation of the ight chambers and tricuspid valve ring

Discussion

In most reports on congenital tricuspid incompetence or Ebstein s anomaly the adio raphic appearances are described as generalized cardiomegaly and diminished pulmonary vascular markings without analysis of specific chamber enlargement (BARRITT & URICH 1956 BARR et coll 1974 BOUCEK et coll 1976 REISMAN et coll 1965 ANTIA & OSUNKOYA 1969) AMPLATZ et coll (1959) analyzed the roentgenologic features of Ebstein s anomaly of the tricuspid valve and pointed out that at l ast the advanced cases have massively dilated right atria and that in such cases the right atrium may form the posterior heart contour in the lateral view as found in the present cases HIPONA & ARTHACHINTA (1965) analyzed 16 cases of Ebstein s anomaly and also pointed out that the enlarged heart had increased convexity in he lower two-thirds of the right cardiac border due to the enlarged right atrium which was also the case in most of the 14 cases analyzed by GENTON & BLOUNT (1967) The present 3 cases of tricuspid insufficiency all had giant right atria and no other entity causing this is known It was therefore considered that the markedly enlarged right atrium at radiography of the chest is diagnostic of massive tricuspid insufficiency with or without concurrent pulmonary atresia Cardiac catheterization and cardioangiography confirm the diagnosis and provide information about associated anomalies and shunts

The marked dilution of contrast medium in the right heart because of the massive tricuspid incompetence and high perinatal pulmonary vascular resistance result in poor filling of the pulmonary artery It is therefore difficult to exclude a concurrent pulmonic stenosis which sometimes exists (BECKER et coll 1971) The presence of systemic right ventricular pressures in one case led us to make the erroneous diagnosis of pulmonic stenosis BARR et coll (1974) made the same mistake because of non filling of the pulmonary artery in the early frames at right ventricular cardioangiography in a case of isolated tricuspid valvular incompetence The diagnosis of pulmonic stenosis can probably only be made if a catheter is advanced into the

pulmonary artery and a gradient is found or an angiography with pulmonary artery injection is performed Pulmonic atresia can be diagnosed if the pulmonary artery is not filled at right ventricular injections (DAVIGNON et coll 1961) Filling of the pulmonary artery during right ventricular cardioangiography excludes pulmonic atresia which is important as prompt surgical intervention is indicated in pulmonic atresia If pulmonic stenosis is possible every effort should be made to enter the pulmonary artery with the catheter to confirm or exclude the diagnosis as the cardioangiographic diagnosis from right ventricular injection is uncertain in our and BARR s experience

BOUCEK et coll (1976) reported about spontaneous resolution of massive congenital tricuspid insufficiency There is no doubt that their cases are similar to the present ones with the exception of a milder clinical course with only mild to moderate congestive heart failure but as in the present cases moderate to severe desaturation of the blood Their catheterization data are similar and their published conventional and cardioangiographic films appear to be identical to the present ones Three of their cases were congenital tricuspid insufficiency of unknown kind possibly so called dysplasia of the tricuspid valve and one case was possibly Ebstein s anomaly All their cases resolved spontaneously with clinical and cardioangiographic evidence of only minimum residual tricuspid insufficiency at examinations up to 3 7 years after birth Although the present cases were severe and all infants died it appears possible to save some of these children with a milder degree of malformation by supportive therapy during their first days or weeks of life Congenital tricuspid incompetence existed in utero in these infants who were born with marked right atrial enlargement and ECG evidence of right ventricular hypertrophy at their first examination immediately after birth They then still had a high pulmonary vascular resistance which made the tricuspid insufficiency more severe and increased the right to left shunt It is probable that the tricuspid incompetence will decrease substantially if the patients can be made to survive the first two weeks of life after which the pulmonary vascular resistance should decrease significantly It can furthermore not be excluded that a dysplastic tricuspid valve may become less dysplastic or even close to normal with growth of the patients so that not only functional but also anatomic improvement occurs The longest survival times for patients with Ebstein s anomaly reported in the literature are 75 and 79 years (HARRIS 1960 ADAMS & HUDSON 1956) and for tricuspid valvular dysplasia 28 and 34 years (BARRITT & URICH 1956)

It is interesting to note but difficult to explain that the degree of dysplasia found at autopsy was reversely correlated to the clinical course of the patients Although the clinical course was severe in all cases it was most severe in Case 3 and least severe in Case 1 with Case 2 falling in between The clinical course may be related to the maturity of the infant as Case 1 was postmature Case 2 term and Case 3 premature

BECKER et coll (1971) described the pathologic spectrum of dysplasia of the tricuspid

he They defined Ebstein s malformation as dysplasia plus downward displacement the basal attachment of one or all leaflets They described three grades of dysplasia d three grades of displacement and the present cases would fall within their oup with grade 3 (Cases 2 and 3) or grade 2 (Case 1) of tricuspid valvular dysplasia ney described one feature common in grade 3 being adhesion of leaflet tissue to e right ventricular wall over often broad areas with or without fenestration of the aflet as seen in Fig 5 of their article The adherent leaflet in their Fig 5 c appears equal a displaced leafl t and it is not obvious what the difference between them In the present Case 3 leafl-t tissue adhered to the right ventricular wall and ereby apparent mild displacement of the leaflet occurred as in the grade 1 displace ent of BECKER et coll In Case 2 there was grade 1 displacement without obvious sion Grade 1 displacement or adhesion of one leaflet is too small a change from e normal to be diagnosed angiographically Apparently there is a broad pathologic ectrum of dysplasia of the tricuspid valve with or without leaflet displacement or dhesion tricuspid dysplasia and Ebstein s anomaly being variations of the same type f disease Fusion and adhesion may basically be the same thing with fusion being e end result of adhesion healed without scar formation Healing without scar ormation is common in fetuses and infants

All cases had gelatinous nodules similar to vegetations 1 to 3 mm in diameter ocated along the free margins and lines of closure of the leaflets These have been escribed by others for example REISMAN et coll (1965) and BARR et coll (1974) he nodular excrescences appear to be larger in Case 1 than those previously escribed and are of unknown origin No inflammatory cells were found in the nodules but they may be post inflammatory The fact that they were found also in he pulmonic valve in two cases may also speak in favor of a post inflammatory tiology Thickened and contracted leaflets and chordae tendineae may appear as equelae of endocarditis As no really satisfactory embryologic explanation of the pectrum of tricuspid dysplasia and Ebstein s anomaly has been given an intra it rine infection as the cause of the disease seems to be an intriguing speculation even if culture in all the present patients was negative) One mother had an influenza like infection in early pregnancy It is interesting to note that it was EBSTEIN s opinion that the anomaly he described was caused by an intrauterine infection (EBSTEIN 1866)

SUMMARY

Three cases of massive congenital tricuspid incompetence in the newborn are reported and discussed from diagnostic pathologic and etiologic points of view The diagnosis is important as cases have been reported with spontaneous resolution

ZUSAMMENFASSUNG

Drei Neugeborene mit einer massiven kongenitalen Tricuspidalinsuffizienz werden beschrieben und von diagnostischen pathologisch anatomischen und atiologischen Gesichtspunkten her diskutiert Die Diagnose ist bedeutungsvoll da Falle mit spontaner Heilung beschrieben worden sind

RESUME

Présentation de trois cas d insuffisance congénitale massive de la tricuspide chez le nouveau né et discussion du point de vue diagnostique anatomo pathologique et étiologique Le diagnostic est important car on a publié des cas de guérison spontanée

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ACUTE HEMIPLEGIA OF CHILDHOOD

H P HATTEN E E KIM F H DELAND and H D JAMESON

The term acute hemiplegia of childhood is used to denote a post natally acquired hemiplegia in a child who was neurologically normal at birth This definition excludes those children with hemiplegia related to prenatal factors e g prematurity birth trauma or perinatal infections Acute hemiplegia of childhood is not a specific disease but rather the non specific response of the central nervous system to injury produced by various etiologies Hemiplegia is the only consistent clinical feature The prognosis other features of clinical presentation and management all depend on the specific etiology producing the acute hemiplegia (CARTER & GOLD 1967)

It is important that this syndrome be recognized to avoid erroneous evaluation of the brain scan but in the literature only few descriptions of the scintigraphic characteristics have appeared (HURWITZ et coll 1973 AITA & KEYES 1974) In children once an abnormal scan consistent with a stroke is identified other features of the clinical history might help toward an appropriate diagnosis

In the child who presents with an acute hemiplegia the initial evaluation should consist of a static brain scan combined with a dynamic evaluation of the initial distribution phase a so-called isotope angiography The dynamic phase will identify abnormal vascularity and may provide a specific diagnosis A review of the etiologies of acute hemiplegia in children is given in the following and the place of scintigraphy in the diagnostic process discussed and illustrated

Infection Many infectious diseases may produce acute hemiplegia in childhood Tuberculous meningitis may produce narrowing and nearly total obstruction of the

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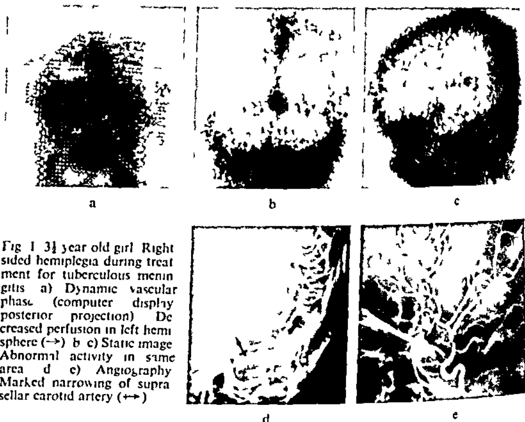


Fig 1 3½ year old girl Right sided hemiplegia during treatment for tuberculous meningitis a) Dynamic vascular phase (computer display posterior projection) Decreased perfusion in left hemisphere (→) b c) Static image Abnormal activity in same area d e) Angiography Marked narrowing of supra sellar carotid artery (↔)

basal and carotid arterial systems and the intracranial branches (GREITZ 1964 GOLD & CARTER 1976) A classical case of tuberculous meningitis with arterial involvement and spasm of the carotid system is illustrated in Fig 1 Bacterial meningitis can produce not only a vascular spasm of sufficient magnitude to cause arterial occlusion but it can also promote sagittal sinus (BICKERSTAFF 1964 SCOTTI et coll 1974) or cortical vein thrombosis with a predilection for one hemisphere (CARTER & GOLD GOLD & CARTER) Hemiplegia is rarely a complication of viral encephalitis but it has been described in patients with encephalitis caused by herpes zoster (WALKER et coll 1973) herpes simplex and coxsackie A9 (GOLD & CARTER) Although the exact mechanism of hemiplegia in viral encephalitis is not known it has been proposed that the inflammation causes focal vasculitis that progresses to occlusive cerebrovascular diseas (GOLD & CARTER)

Retropharyngeal infection has long been implicated as a cause of hemiplegia fror an arteritis produced by direct extension of the inflammation and the proximity of th internal carotid system (SHILLITO 1964 HARWOOD NASH et coll 1971) Althoug this theory has not been definitely documented clinical observations have been mad repeatedly of acute hemiplegias in childhood frequently associated with retro pharyngeal and paratonsillar inflammation

Systemic diseases have been associated with hemiplegia in children In children wit homocystinuria progressive cardiovascular disease and a high frequency of thrombo

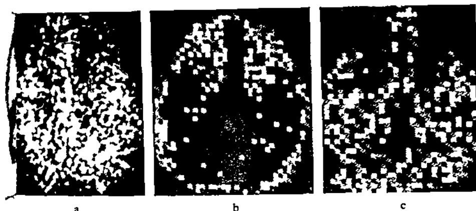


Fig. 2 Migraine in a 10 year old boy with a ? year history. Right hemiplegia. a) Initial dynamic phase 3 days later following a migraine attack (vertex projection). b, c) ?½ months later (computer display). Persistent abnormality in same region.

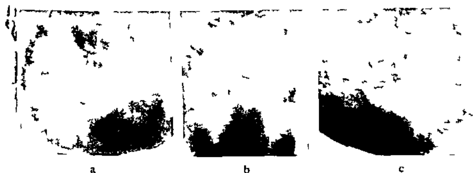


Fig. 3 Emboli following surgery. Static images demonstrate abnormal activity in regions vascularized from right and left middle cerebral artery. (Dynamic phase demonstrated markedly decreased perfusion to right and left hemispheres.)

embolism is well documented (HARKER et coll. 1974). Systemic lupus erythematosus in children can produce acute hemiplegia (COOK et coll. 1960); however, polyarteritis nodosa rarely results in acute hemiplegia in children (ROBERTS & FETTERMAN 1963). As many as 15 per cent of children with sickle cell disease will develop hemiplegia (PORTNOY & HERION 1972) that may be secondary to small or large vessel occlusion (STOLLMAN et coll. 1972). Children with leukemia (GROCH et coll. 1960), hemophilia and idiopathic thrombocytopenia purpura are prone to intracranial hemorrhage (GOLD & CARTER).

Hemiplegic migraine is a paroxysmal episode of vascular instability characterized by vasodilatation and vasoconstriction. During a migraine attack, vasoconstriction has been documented by means of ^{133}Xe cerebral blood flow measurement (SKINHOJ & PAULSEN 1969, O'BRIEN 1971) and by angiography (DUKES & VIETH 1974).

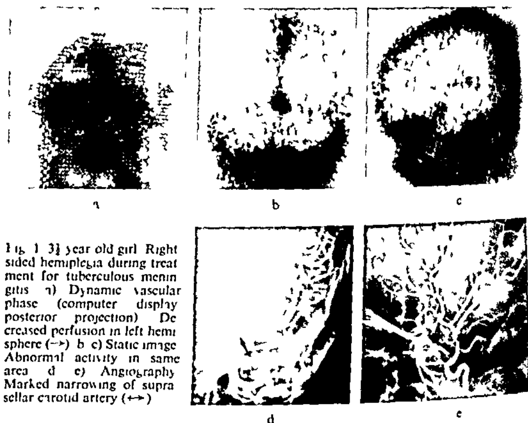


Fig. 1. 3½ year old girl. Right sided hemiplegia during treatment for tuberculous meningitis. a) Dynamic vascular phase (computer display posterior projection). Decreased perfusion in left hemisphere (→). b, c) Static image. Abnormal activity in same area. d, e) Angiography. Marked narrowing of suprasellar carotid artery (↔).

basal and carotid arterial systems and the intracranial branches (GREITZ 1964, GOLD & CARTER 1976). A classical case of tuberculous meningitis with arterial involvement and spasm of the carotid system is illustrated in Fig. 1. Bacterial meningitis can produce not only a vascular spasm of sufficient magnitude to cause arterial occlusion but it can also promote sagittal sinus (BICKERSTAFF 1964, SCOTTI et coll. 1974) or cortical vein thrombosis with a predilection for one hemisphere (CARTER & GOLD, GOLD & CARTER). Hemiplegia is rarely a complication of viral encephalitis, but it has been described in patients with encephalitis caused by herpes zoster (WALKER et coll. 1973), herpes simplex and coxsackie A9 (GOLD & CARTER). Although the exact mechanism of hemiplegia in viral encephalitis is not known, it has been proposed that the inflammation causes focal vasculitis that progresses to occlusive cerebrovascular disease (GOLD & CARTER).

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Systemic diseases have been associated with hemiplegia in children. In children with homocystinuria, progressive cardiovascular disease and a high frequency of thrombo

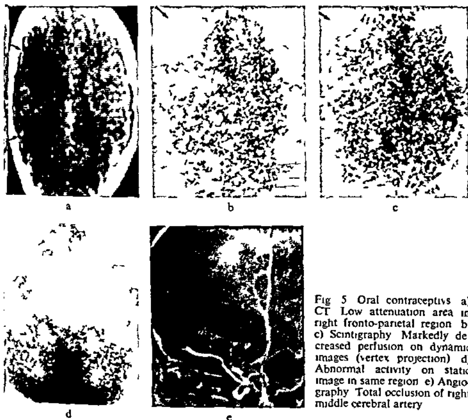


Fig 5 Oral contraceptivs a) CT Low attenuation area in right fronto-parietal region b c) Scintigraphy Markedly decreased perfusion on dynamic images (vertex projection) d) Abnormal activity on static image in same region e) Angiography Total occlusion of right middle cerebral artery

(MASI & DUGDALE 1970) Normally oral contraceptives would be considered unusual in the pediatric age group however one example is demonstrated in Fig 5

Trauma Contusions epidural hematomas may produce hemiplegia (CARTER & GOLD GOLD & CARTER) In children acute hemiplegia results from non penetrating trauma to the paratonsillar area (BRAUDO 1956 FAIRBORN 1957) Usually the child falls with a pencil or other pointed object in the mouth and causes small intimal tears in the internal carotid artery because of its anatomic proximity to the tonsillar bed These intimal tears serve as a nidus for thrombosis formation with subsequent propagation of thrombus distally into the intracranial circulation Characteristically a latent period exists between injury and development of acute hemiplegia (PITNER 1966) External trauma to the neck or head may also be associated with a hemiplegic state (FRANTZEN et coll 1961) and a similar mechanism for thrombus formation has been proposed

Structural abnormalities of vessels The most common vascular anomaly in children is arteriovenous malformation and its usual clinical presentation is signs of cerebral hemorrhage (MOYES 1969) Congenital intracranial aneurysms (berry aneurysms)

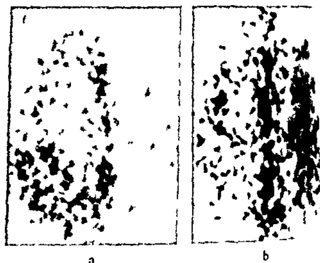


Fig 4 Emboli following surgery Dynamic image of initial scintigraphy (vertex projection) Markedly diminished perfusion in left hemisphere (static images were normal) Repeat scintigraphy 5 days later revealed normal dynamic and static images

The term complicated migraine is used to denote the appearance of transient neu[illegible] ogic deficit during and following a migraine episode Such a neurologic deficit most commonly present as an intermittant hemiparesis is transitory and will usually resolve within 48 hours (GOLDEN & FENICHEL 1975) Although pareses do not occur as sequelae to complicated migraine episodes a high incidence of residual mental retardation and movement disorders is observed (VERRET & STEELE 1971) In th[illegible] illustrated case (Fig 2) complete resolution of hemiplegia required 4 months

Emboli Although a number of cardiac conditions in children predispose to th[illegible] formation of emboli vascular occlusion from emboli is relatively uncommon

Rheumatic heart disease frequently associated with atrial fibrillation is a common sourse of emboli (FORD 1973) The most common central nervous system complication of bacterial endocarditis is cerebral vascular occlusion (JONES et coll 1969) These patients may also develop an acute meningitis or a toxic encephalopathy (TOONE 1941) Certain types of congenital heart disease are associated with cerebral emboli (TYLER & CLARK 1957) but the highest incidence of cerebral vascular occlusion is found in those patients with congenital heart disease that produce polycythemia After o[illegible] during open heart surgery air emboli or thromboemboli (GLIMAN 1965) may develop secondary to a number of causes (Figs 3–4) Although fat emboli are an unusual cause of cerebral vascular occlusion, as many as 33 per cent of patients with the syndrome of fat embolism will develop focal signs of the central nervous system (THOMAS & AYYAR 1972) Most common are multiple micro emboli (EVARTS 1970), however large fa[illegible] globules can produce vascular occlusion (FELDMAN et coll 1975) Air emboli can occur secondary to pneumothorax thoracocentesis thoracic surgery (COHEN et coll 1951) and open heart surgery (GILMAN) Cardiac myxomas rarely produce cerebral emboli (CARTER & GOLD)

Women taking oral contraceptives have a well documented and significant morbidity and mortality secondary to cerebrovascular thromboembolic complication

hich may be multiple are rare in children (MATSON 1965 LEBLANC et coll 1968) and ave been associated with aortic coarctation (LEBLANC et coll) and polycystic renal isease Dissecting aneurysms of the internal carotid arteries or intracranial arterial stem with or without arterial medial necrosis (WOLMAN 1959 WISOFF & ROTH ALLER 1961) are also rare causes of acute hemiplegia in childhood

Moyamoya syndrome In the Moyamoya syndrome the angiographic appearance is pathognomonic characterized by narrowing or occlusion of both internal carotid rteries and diffuse telangiectasia of the arterial system in the basal ganglia (TAVERAS & WOODS 1976) Originally this syndrome was thought to occur exclusively in the Japanese but now is known to occur in the black and white races as well Recent reports on this syndrome have revealed a malignant clinical course with progressive motor and intellectual deficits (CARLSON et coll 1973)

Idiopathic hemiplegia In a large number of children with acute hemiplegia no precise etiology can be identified (DAVIE & COXE 1967) Arterial thrombosis has been documented in 40 per cent of this group (GOLD & CARTER) and localized arteritis may represent the cause in others Despite the inability to elicit a specific cause for hemiplegia in these children it is important to define the level of vascular occlusion that produced the hemiplegia for the prognosis One example is given in Fig 6

Comment The syndrome acute hemiplegia of childhood denotes a post natally acquired hemiplegia in a child who was neurologically normal at birth The hemiplegia is a non specific response of the central nervous system to a number of different etiologies *For the initial evaluation of these cases* dynamic and static cerebral scintigraphy should be the initial examinations Since prognosis and treatment depend upon the underlying cause of the acute hemiplegia it is important to define the level of vascular occlusion producing the acute hemiplegia After scintigraphy cerebral angiography and computer tomography are important complementary examinations

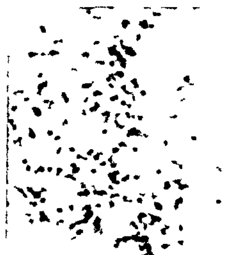
SUMMARY

Acute hemiplegia of childhood is briefly reviewed with examples of various etiologies The role of brain scans in diagnosing and following children with this syndrome is emphasized Cerebral angiography and computer tomography represent complementary examinations in the evaluation of these patients

Fig 6 Idiopathic hemiplegia in a 7 year-old boy a, b) Angiography Almost complete occlusion of left middle cerebral artery (→) c d) Initial dynamic scintigraphy Markedly diminished perfusion in region vascularized from left middle cerebral artery corresponding abnormal activity in static image e f) Scintigraphy one year later was normal but the patient had a persistent right sided minor neurologic def cit


a


b


c


d


e


f

Fig 6 (For legend s e opposite page)

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ZUSAMMENFASSUNG

Akute Hemiplegie im Kindesalter wird kurz zusammenfassend beschrieben mit Beispielen verschiedener Ätiologien Die Bedeutung von Gehirnszintigraphie bei der Diagnose und der Nachuntersuchung von Kindern mit diesem Syndrom wird hervorgehoben Cerebrale Angiographie und Computertomographie bilden zusatzliche Untersuchungen bei der Beurteilung dieser Patienten

RESUMÉ

Les auteurs font un bref rappel de l hémiplégie de l enfance et donnent des exemples des différentes étiologies Ils insistent sur l importance des gamma encéphalographies pour le diagnostic et la surveillance des enfants qui sont atteints de ce syndrome L angiographie cérébrale et la tomodensitométrie sont des examens complémentaires dans l étude de ces malades

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Fig 1 Patient positioned in the plastic cradle before the examination

ml kg body weight with a maximum dose of 1 5 ml to children with a weight exceeding 15 kg The dose was reduced if the condition of the child so required If necessary 25 to 50 per cent of the initial dose was added intravenously during the examination In order to facilitate additional sedation or intravenous injection of contrast medium a cannula was introduced in a suitable vein in the ward Newborns and infants were fed before the examination with the purpose to make them satisfied and sleepy Small children were examined in a cradle designed to support both the head and the body (Fig 1) The cradle was made of a 4 mm thick plastic material (Cabulite) which does not cause any artifacts of the image The cranial part of the cradle was slightly tilted to give a desirable scanning angle of about 20 degrees to the orbitomeatal line The position of the scanning sections was indicated on the cradle The head of the baby was strapped to the cradle with an elastic band and the cradle then attached to the opening of the scanner with screws The air space between the head and the cradle may be filled with pieces of cloth or rubber foam to immobilize the head However it was possible to scan in spite of a rather large air space if the potential of the PM tubes was decreased to avoid over range

An EMI Mark I CT scanner with a water box and an 160 × 160 matrix was used The scanning time was 5 min and the potential 120 kV An 8 mm collimator was used for patients below one year of age and a 13 mm collimator for older children

The radiation doses to 9 infants were measured with thermoluminescent (TL) rods The TL rods were attached to the skin (a) on both sides and anteriorly of the head (b) on both sides of the neck at the level of the thyroid gland (c) anteriorly on both sides of the abdomen at the level of the ovaries (d) at the level of the testicles and (e) on both sides of the scanner behind a lead apron (0 25 mm lead) For the

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COMPUTER TOMOGRAPHY OF THE HEAD IN CHILDREN

Technical aspects

U ERASMIE and M BERGSTRÖM

Computer tomography has proved to be a highly accurate non invasive neuro radiologic examination technique However for children precautionary measures are needed to obtain optimum information and minimum radiation dose The aim of this report is to draw attention to the problems involved in the examination of children and to report on the experiences with a modified examination routine

Material and Methods

Computer tomography was performed in 186 children 76 below one year, 44 between one and 5 years 38 between 5 and 10 years and 28 between 10 and 15 years. At the beginning 21 patients were examined under general anesthesia two thirds being between one and 5 years In the remaining 165 sedation of the patient by means of a mixture of promethazine 6 25 mg/ml chlorpromazine 6 25 mg/ml and meperidine 25 mg/ml was sufficient for obtaining satisfactory results of the examination Intra muscular sedation was employed 1 hour before the examination with a dosage depending on body weight and condition of the child The ordinary dose was 0 1

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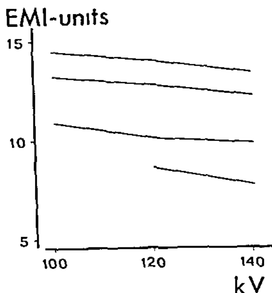


Fig. 2. Difference in attenuation between brain tissue and CSF at different potentials in 4 cases

are given in the Table The doses to an assistant beside the scanner are given in the same Table The measurements on the cadavers revealed a mean dose of 4 8 mGy at the thyroid gland without protection and 4 3 mGy with lead protection The average skin dose without protection was 3 9 mGy The variations in measured doses are insignificant The mean attenuation values of brain tissue was observed for an increase in potential of 20 kV for CSF the corresponding decrease was 0 7 EMI units The relation between the attenuation values of brain tissue and CSF at different potentials is given in Fig 2 The difference decreased at the mean 0 6 EMI units for an increase of 20 kV In all cases the largest differences were obtained at 100 kV At 120 kV the difference was 11 4 $\pm$ 2 5 EMI units (1 SD) In one patient the values at 100 kV were not used because of large artifacts

Discussion

The introduction of CT scanning implied a major improvement in neuroradiology The procedure is painless and safe which is of particular value in pediatric practice For a successful scanning the patient must remain immobile during the examination For this reason infants usually have been examined under general anesthesia (AIDINIS et coll 1976) which has limited the use of the method However it is possible to examine most infants without general anesthesia by means of simple sedation and immobilization (HOLSER et coll 1975 NAIDICH et coll 1976)

The development of scanners with a short scanning time and without water bag will further facilitate the procedure A mixture of promethazine chlorpromazine and meperidine has been widely used for sedation of children before different radiologic

Table

Radiation doses per examination in 9 cases and one assistant

Site	Dose (mGy)
Skull right	34±18
Skull left	15±9
Skull anteriorly	13±6
Thyroid right	4 3±3 3
Thyroid left	2 6±1 9
Gonads females	0 48±0 48
Gonads males	0 13±0 12
Assistant	
on patient s right	0 04±0 03
on patient s left	0 06±0 07

(1 mGy = 100 mrad)

latter measurements the same dosimeters were used during several examinations in order to get an accurate reading The results in these cases were recalculated to doses from one examination consisting of 4 scans Dose measurements were also performed on 2 cadavers of neonates in both lateral lobes of the thyroid gland with and without shielding and on both sides of the skin over the thyroid gland The shielding consisted of lead rubber (0 25 mm lead 7 cm × 13 cm) covering the anterior part of the neck

In 4 children the same section was scanned with three different settings of the potential 100 120 and 140 kV Using 80 × 80 matrix print outs the mean attenuation was calculated for regions of brain tissue (mixed white and grey) cerebral spinal fluid in the lateral ventricles and water outside the head

Care was taken to ascertain that the same regions were used for the different potentials and that they were unaffected by artifacts The attenuation values of water were subtracted from those of brain tissue and CSF and the result was plotted against voltage This was also done for the difference between brain tissue and CSF

Results

It was impossible to carry out the examination in 13 patients (8 below one year and 5 between one and 5 years) because they were not at ease In 3 of them the examination was later carried out under general anesthesia but in 5 cases the examination was successfully repeated under the usual sedation at a later occasion Accidentally an overdose of the sedative mixture was administered to one patient resulting in depressed respiration and cyanosis The patient recovered in a few hours without special measures No other complications were encountered

The mean radiation dose per examination and standard deviation in 9 patients

SUMMARY

A modified routine for computer tomography of children avoiding general anesthesia discussed The patients were sedated and examined in a supporting plastic cradle Radia n doses to various parts of the body were measured during the scanning and the results nfirm that the dose levels are within generally accepted limits

ZUSAMMENFASSUNG

Eine geanderte Routine fur die Computertomographie von Kindern ohne Anwendung n Vollnarkose wird diskutiert Die Patienten wurden sediert und in einer Plastikwiege itersucht Die Strahlendosen fur die verschiedenen Abschnitte des Korpers wurden wah nd der Szintigraphie gemessen und die Ergebnisse bestatigen dass die Strahlendosen inerhalb allgemein akzeptierter Grenzwerte liegen

RÉSUMÉ

Les auteurs examinent une methode pratique de tomographie avec ordinateur chez l enfant vitant une anesthésie générale Les malades subissent une sédation pharmacologique et ont examinés dans un support berceau en plastique Les doses de radiations aux differentes arties du corps ont été mesurées pendant l examen et les résultats confirment que les niveaux le doses sont dans les limites généralement acceptées

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examinations especially cardiac catheterization and was found to be adequate also for CT scanning (ANDERSON & OSBORN 1977) No serious complications occurred in their material of several hundred cases Also in the present series this mixture was found to be adequate for sedation and no serious complications occurred As the mixture is potent, it is necessary to reduce the dose in patients with severe constitutional symptoms Careful supervision is self evident In spite of sedation the child is fed before the examination in order to become satisfied and sleepy

The radiation doses were low lying within the limits generally accepted for diagnostic radiology As the roentgen tube moves on the right side of the scanner the doses to the right side of the body are higher than those to the left However the dose to the left side of the head is higher than to the anterior part which probably is due to the influence of the large air spaces on both sides of the head

The radiation dose may be reduced further by decreasing the tube potential However the dose reduction will be at the expense of a higher noise level and thus a poorer image quality

Around the scanner the scattered radiation is highest on the left side This might be different for different scanners and is for instance depending on the shielding of the roentgen tube (PERRY & BRIDGES 1973) A person attending the patient during the examination should consequently be placed on the right side of the patient wearing a lead apron Recorded values for thyroid and gonadal doses are in good accordance with those reported by BHAVE et coll (1977) The level of the radiation dose and its distribution results from the construction of the scanner used and may vary markedly in different scanners (BRASCH et coll 1977) Reports on radiat or doses from other neuroradiologic procedures are rare BERGSTRÖM et coll (197 measured the lens dose at carotid angiography and found an average dose of 1(mGy The dose could be reduced to 59 mGy in average by using a lens shield Q is LING et coll (1974) reported a mean lens dose of 125 mGy and a gonadal dose ran in from zero in most cases to 0 3 mGy with one extreme value of 44 mGy

Attempts to shield the thyroid gland using lead rubber gave no significant decreas This is probably due to the fact that the main contribution to the dose comes fro scattered radiation which reaches the thyroid glands from an obtuse angle

The possibility of increasing the contrast between tissues by changing the potenti of the roentgen tube has been discussed previously (CHO et coll 1975 PHELPS et co 1975) Measurements of the attenuation at different settings of the potential show that both the attenuation for brain tissue and for CSF decreased with increas potential This was also the case for the difference between brain tissue and CS An increase of 20 kV caused a decrease in the difference of about 0 6 EMI units systematic error from the spectral shift artifact could have influenced this figu although attempts were made to locate the regions of interest away from bon Hence a very little gain in contrast between brain tissue and CSF is obtained l lowering the potential Furthermore lowering the potential will increase the noise the images

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DIAGNOSIS

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LABELLING METRIZAMIDE (AMIPAQUE) WITH IODINE-125

H L SHARMA and A G SMITH

Metrızamıde [2 (3 acetamıdo 5 N methylacetamıdo 2 4 6-trııodobenzamıdo) 2 de ɔxy D glucose] ıs a non ıonıc water soluble radıographıc contrast medium (Acta ʻadıol (1973) Suppl No 335) For varıous ınvestıgatıons requırıng hıgh sensıtıvıty g excretıon dıstrıbutıon and retentıon formatıon of metabolıtes etc the use of the radıoıodıne labelled compound ıs necessary Although the Chemıcal Research Department of Nyegaard & Co Oslo Norway has synthetızed metrızamıde using ^{12}I ıt ıs not wıdely avaılable The aım of thıs communıcatıon ıs to descrıbe an efficient method of labellıng metrızamıde with ^{1} I by ısotopıc exchange ın aqueous solutıon

Materıal and Method

(1) Amıpaque containing metrızamıde (6 75 g) and sodıum calcıumedetate (2 2 mg) a freeze-drıed sıngle dose unıt (2) Solvent for Amıpaque contaınıng sodıum bı carbonate (5 mg/100 ml) ın sterıle aqueous solutıon (3) $^{1-5}$I as ıodıde 3 7 GBq (100 mCı) per ml carrıer free ın NaOH solutıon pH 8–11 free from reducıng agent (100 mCı/ml) (Radıochemıcal Centre Amersham England) (4) Solutıon of $CuSO_4$ $5H_2O$ in water (4 mg/ml) (5) Amberlıte resın CG-400 (Cl) (BDH Chemıcals Ltd Poole England) (6) Zerolıte 225 SRC 13 (standard catıon exchange resın) (BDH Chemıcals Ltd)

From the Department of Medical Bıophysıcs Unıversıty of Manchester Manchester M13 9PT England. Submıtted for publıcatıon 1 September 1978

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ZUSAMMENFASSUNG

Eine Methode zur Markierung von Metrizamid mit I wird beschrieben

RESUME

Description d une methode pour marquer le métrizamide avec ^{125}I

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METRIZAMIDE a non ionic water soluble contrast medium Experimental and preliminary clinical investigations Acta radiol (1973) Suppl No 335

Experimental In the early experiments one gram of Amipaque was dissolved in 3 ml of the solvent and transferred to a 10 ml vial To this was added a 0 5 ml solution of copper sulphate and 37 MBq (1 0 mCi) of ^{125}I The vial was left in a water bath at 50 C for overnight ($\sim$16 h) The bath was covered to keep the solution in the dark The solution was passed through an anion exchange column (Amberlite resin) to remove the free iodine No activity was observed on the column The solution was washed free of Cu^{++} ions by passing it through a cation exchange column containing Zerolite 225 resin

Although the labelling efficiency was 100 per cent in this procedure the danger of hydrolysis of the compound existed because of the long time involved in the procedure as well as an additional danger of Cu^{++} ions altering the chemical structure of the metrizamide Subsequent experiments revealed that greater than 90 per cent labelling can be achieved with 0 1 ml $CuSO_4$ solution and 4 hours labelling time

In order to check the integrity of the metrizamide molecule, thin layer chromatographic procedure was employed which is identical to the TLC system 2 of FREY (1973) A minute drop of the labelled compound was applied on Silica gel F_{254} TLC plates Merck and dried gently under an airstream The plates were developed in a solvent of chloroform methanol (80–20) After development and drying the plate was cut into 1 cm strips and counted using a scintillation counter The unchanged metrizamide the lowest strip (R_f 0–0 15) contained all the activity No other strip showed any activity

A final check on the integrity of the molecular composition of the labelled metrizamide was made by the Research Department Nyegaard & Co which confirmed the results

Routine preparation For routine preparation a suitable quantity of Amipaque is weighed and dissolved in the appropriate amount of Amipaque solvent The solution is transferred to a vial To this are added 0 1 ml of copper sulphate solution and the required amount of ^{125}I The vial is kept in the covered water bath at 50 C for 3 to 4 hours The free iodine is removed by passing the solution through an anion exchange column (Amberlite CG 400 (cl) and finally Cu^{++} ions are removed by a cation exchange column (Zerolite 225) The solution is millipore filtered before use

Acknowledgements

The authors wish to thank Professor B R Pullan Department of Medical Biophysics and Professor I Isherwood Department of Diagnostic Radiology University of Manchester for stimulating the work and The Research Department of Nyegaard & Co Oslo Norway for providing the materials and testing the labelled product

SUMMARY

A method for labelling metrizamide with ^{125}I is described

uracy of the method in diagnosing these thrombi were sufficiently great it would e of considerable importance in the prevention of emboli The present comparison was designed to evaluate the diagnostic accuracy of ultrasound and clinical examination Phlebography was performed at the same time to establish the final diagnosis

Material and Methods

Fifty-eight patients 35 women and 23 men with a mean age of 69 years gave heir consent to taking part in the trial Of these 40 patients had undergone surgery of the abdomen or chest and 18 patients surgery of the hip 15 of these for fracture of the femoral neck

Eighteen patients had been referred with a clinical suggestion of deep vein thrombosis Two were examined after a massive pulmonary embolism without simultaneous signs of thrombosis of the legs The remaining 38 patients had no symptoms or signs of either pulmonary embolism or thrombosis

In 4 patients varices were detected preoperatively and 2 had a history of phlebitis

Clinical evaluation All patients were evaluated for the following 5 signs (1) Soreness of the calf or a positive Homan s sign (2) Venostasis of a horizontal leg with the patient supine (3) Oedema determined by measuring the thickest point of the calf or by an appraisal in cases of bilateral changes (4) Local heat of the leg as evaluated by palpation with the back of the hand (5) Increased body temperature (>38 C)

A deep vein thrombosis was considered possible if one of the first four signs was present and probable if 2 of the 5 signs were present

Ultrasound examination A portable Siemens type E 2019 apparatus (frequency 5 MHz output power 20 milliwatt with radiation surface of transducer 16 mm²) was used and Ultrasound paste between transducer and patient (Aguasonic Parker)

The first site to be examined was the femoral artery just below the inguinal ligament where a distinct pulse synchronous sound was heard Just medial to this point the femoral vein is located On listening over the vein a respiration synchronous S sound may be heard which is caused by the flow rate and filling of the vein varying with the respiratory rate This sound indicates free passage in the veins between the auscultation point and the heart

If pressure is applied on the femoral vein distally to the auscultation spot or on the calf veins a pulse wave is produced in the vein which is recorded as an A sound with a higher frequency than the S sound This A sound is only heard if no obstruction exists between the spot where the pressure is applied and the auscultation point

Presence of an S sound was tested in all patients Pressure applied distally on the thigh above the femoral vein compression of the crural veins and finally bending the foot backwards were used to demonstrate the A sound Absence of an S sound was considered to indicate an obstructed passage caused by thrombosis of the iliac veins and absence of an A sound an obstruction between the spot where the pressure was

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ULTRASOUND AND CLINICAL DIAGNOSIS OF DEEP VEIN THROMBOSIS OF THE LEG

J KIIL and J C MØLLER

Deep vein thrombosis cannot be detected with sufficient accuracy by clinical evaluation alone because large numbers of both false positives and false negatives occur (HAEGER & NYLANDER 1967 HAEGER 1969 BRODELIUS et coll 1970 MILNE et coll 1971) This is in accordance with the fact that only a minority of patients dying from pulmonary embolism have symptoms of thrombosis of the leg prior to the embolism (SEVITT & GALLAGHER 1961 LAMBIE et coll 1970 WILLIAMS 1973)

Phlebography is considered the most accurate technique for demonstration of thrombosis (WILLIAMS LE QUESNE 1974) This examination involves however a certain amount of discomfort since it requires insertion of a cannula into a foot vein and it cannot be carried out at the bedside Therefore the method is not appropriate for repeated observations

^{125}I fibrinogen scanning is based on the principle that the labelled fibrinogen is built into thrombi under formation (HOBBS 1961, ATKINS & HAWKINS 1965) With simple measuring equipment the thrombi can be demonstrated at the bedside as well as their development by repeated examinations However the majority of thrombi detected by this method are quite small and only thrombi below the middle of the thigh are demonstrated with sufficient certainty (BROWSE 1972 HEDLUND 197

Ultrasound examination is non traumatic requires only simple measuring equipment, and can be used at the bedside Only thrombi in the popliteal vein and in the more proximal large veins can be demonstrated It is precisely in this region the pulmonary emboli originate (HAEGER & NYLANDER BRODELIUS et coll) If the a

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Table 2

Calculation of diagnostic specificity and diagnostic sensitivity of ultra sound examination clinical evaluation and a combination of both The calculations were performed on the basis of the figures in Table 1 95 confidence limits within parentheses

	Diagnostic specificity	Diagnostic sensitivity
1—Ultrasound	$\frac{8}{11}$ 0.73 (0.39–0.94)	$\frac{31}{4}$=0.70 (0.55–0.83)
2—Clinical evaluation	$\frac{13}{18}$=0.72 (0.46–0.90)	$\frac{31}{4}$=0.78 (0.62–0.89)
3 a—Combination of 1 and 2 both abnormal for a diagnosis of thrombosis	$\frac{7}{8}$=0.88 (0.47–1.00)	$\frac{5}{40}$=0.70 (0.55–0.82)
3 b—Combination of 1 and 2 no abnormality for exclusion of thrombosis at both	$\frac{14}{1}$=0.67 (0.43–0.85)	$\frac{9}{37}$=0.78 (0.62–0.90)

The results of the ultrasound and clinical examinations agreed in 45 cases When compared with the phlebographic diagnosis the results of both ultrasound and clinical evaluation were correct in 36 cases and erroneous in 9 In 13 cases different results were obtained at ultrasound and clinical evaluation Of these ultrasound gave the same result as phlebography in 5 cases and clinical evaluation the same as phlebography in 8 cases This difference is not significant ($p > 0.05$)

In the 9 cases of false normal results at the clinical examination and in 13 of 14 false normal results at ultrasound phlebography showed thrombosis without total venous occlusion In the remaining case with a false normal result at ultrasound complete obstruction of the femoral vein with an ample collateral network was found at phlebography presumably this network was caused by a previous thrombosis

False abnormal clinical findings were encountered in 5 patients Two of these had been operated upon for fracture of the femoral neck and another had undergone hip replacement because of arthrosis One of the false abnormal ultrasound examinations was also found in a patient operated upon for fracture of the femoral neck The remaining false abnormal examinations occurred in patients with abdominal surgery In one of these a tumour growth was found compressing the external iliac vein

Nin of the 22 patients with thrombosis had bilateral thrombi and 21 had thrombosis in or proximal to the popliteal vein

Sid effects Phlebography was associated with transitory pain of the calf and soreness along the veins in 4 of the first 22 patients and with bilateral superficial phlebitis in one patient The technique was then changed After completion of the

Table I

Results of ultrasound and clinical evaluation in 58 patients

	Clinical evaluation	
	Abnormal	Normal
Phlebography abnormal (22 patients)		
Ultrasound abnormal (8 patients)	7	1
Ultrasound normal (14 patients)	6	8
Phlebography normal (36 patients)		
Ultrasound abnormal (3 patients)	1	2
Ultrasound normal (33 patients)	4	29

applied and the auscultation spot A weaker sound on one side was also considered an indication of venous occlusion

Phlebography In the supine patient a vein on the dorsum of the foot was punctured with a thin cannula (Butterfly Abbott Ireland Ltd , 1 1 mm) and 50 to 100 ml of Isopaque Amin (meglumine calcium metrizoate 280 mg I/ml) was injected The head end of the couch was elevated 30 to 60 degrees No support to the leg being examined and no tourniquet was applied When the veins were filled as assessed by fluoroscopy films were exposed of the calf veins popliteal vein, femoral vein and iliac vein on both sides If thrombi were demonstrated the injection was repeated and new films exposed in a perpendicular plane A clear defect preferably surrounded by contrast medium in an otherwise well filled vein was considered to be a certain thrombosis as was also a cupola over the proximal border in the case of total occlusion of the vein Filling of only the superficial veins combined with the clinical signs was also considered a certain indication of deep vein thrombosis

The clinical examination was performed first followed by the ultrasound and then phlebography which was carried out without knowledge of the result of the other two examinations The results of all three examinations were compared after the report on the phlebography Since a comparison between the sounds from the two legs was necessary to allow an assessment of the ultrasonic examination the evaluation of the investigation was based on the number of patients not the number of legs

The diagnostic specificity and the diagnostic sensitivity (WULFF 1976) of the clinical and ultrasound examinations were calculated by comparing the results of each method with the findings at phlebography

Statistics In the comparison between the results of the examinations $p < 0\ 05$ was chosen as the significant level The confidence limits are the 95 per cent limits

Results

The results appear in Table 1 On the basis of these figures the diagnostic specificity and the diagnostic sensitivity were calculated for the ultrasound examination the clinical evaluation and for both together (Table 2)

Phlebography is the only certain method for diagnosing deep vein thrombosis (WILLIAMS LE QUESNE). A diagnosis of deep vein thrombosis involves prolonged anticoagulant therapy with frequent controls and risk of haemorrhages. These possible complications seem to justify a broader use of phlebography. It should be a definite rule that anticoagulant therapy is not instituted unless the diagnosis is confirmed at phlebography. It cannot be replaced by the simpler but less specific and sensitive ultrasound or ¹²⁵I fibrinogen scanning methods.

SUMMARY

The diagnostic precision of clinical evaluation and of ultrasound examination in the diagnosis of deep vein thrombosis was obtained by ascending phlebography. The diagnostic specificity and diagnostic sensitivity of clinical examination was 0.72 and 0.78 and with ultrasound 0.73 and 0.70. With no other examination than phlebography is it possible to demonstrate major central thrombosis in the leg with certainty.

ZUSAMMENFASSUNG

Die diagnostische Genauigkeit der klinischen Untersuchung und der Ultraschall Untersuchung bei der Diagnose von tiefen Venenthrombosen wurde mit der aszendierenden Phlebographie verglichen. Die diagnostische Spezifität und die diagnostische Empfindlichkeit der klinischen Untersuchung betrug 0.72 und 0.78 und mit Ultraschall 0.73 und 0.70. Mit keiner anderen Untersuchung als Phlebographie ist es möglich eine umfassende zentrale Thrombose im Bein mit Sicherheit nachzuweisen.

RESUMÉ

La phlébographie ascendante a permis de déterminer la précision diagnostique de l'examen clinique et de l'examen échotomographique dans le diagnostic de la thrombose des veines profondes. La specificité diagnostique et la sensibilité diagnostique de l'examen clinique ont été de 0.72 et 0.78 et celles des ultra sons de 0.73 et 0.70. Sans autre examen que la phlébographie il est possible de mettre en évidence avec certitude les thromboses centrales importantes du membre inférieur.

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phlebography, physiologic saline was infused Thereafter no pain occurred in the last 36 patients No clinical pulmonary embolism was encountered in connection with the injection

Discussion

Since lung emboli originate from veins above the level of the popliteal vein (HAEGER & NYLANDER BRODELIUS et coll) ultrasound examination would be an ideal method for repeated examination of patients who are particularly at risk for thromboembolic complications It is non traumatic rapidly performed and active participation of the patient is not necessary The equipment is inexpensive and easy to move The present results show however that the diagnostic accuracy is not better than that obtained by clinical evaluation alone Partial thrombosis of large veins cannot be demonstrated either by the ultrasound or by the clinical evaluation In the two patients with severe pulmonary embolism neither ultrasound nor the clinical examination indicated any abnormality despite the fact that phlebography revealed freely floating thrombi of a length of more than 10 cm in both patients In one of them the thrombus was removed surgically

The ultrasound examination has been reported to be both more specific and more sensitive than the present results would suggest (STRANDNESS & SUMNER 1972 EGEBLAD & DLIGACZ 1976) All their patients had clinical evidence of thrombosis which might explain their better results However the present results do not suggest that this examination would be particularly useful in such patients Thus we found a diagnostic specificity of $\frac{7}{8}$=0 88 (0 47–1 00) and a diagnostic sensitivity of only $\frac{4}{10}$=0 40 (0 12–0 74) when the values were calculated alone on the basis of the 18 patients with clinical signs of deep vein thrombosis The present results agree with those reported by MILNE et coll who screened patients at risk without symptoms They found ultrasound to offer no advantage over ordinary clinical evaluation

The false normal results at ultrasound examination and clinical evaluation were encountered in cases with thrombi causing only partial obstruction The most frequent cause of false abnormal results at clinical evaluation was that patients with hip operation often developed oedema and soreness of the thigh extending along the medial side thus making distinction from a venous thrombosis impossible

It might be supposed that ultrasound combined with clinical evaluation would increase the diagnostic accuracy but the calculations in Table 2 show a relationship between diagnostic specificity and sensitivity If it is required that abnormality be found at both examinations for a certain diagnosis of thrombosis a high specificity is obtained but at the same time the sensitivity decreases (3 a of Table 2) conversely if no abnormality is required for exclusion of a thrombosis a high sensitivity is obtained but the specificity diminishes (3 b of Table 2)

^{125}I fibrinogen scanning is unable to detect thrombi in the vascular region viz proximal to the middle of the thigh (BROWSE HEDLUND) thus this method is unsuitable for examination for embolism threatening thrombi (SEVITT & GALLAGHER LE QUESNE)

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HEPATOBILIARY SCINTIGRAPHY WITH $^{99}Tc^{m}$-HIDA IN PATIENTS WITH JAUNDICE

E ØSTER JORGENSEN S A PEDERSEN and J SCHOUBYE

For several decades scintigraphic imaging of the liver and biliary tract has been carried out with a rectilinear scanner using variously labelled hepatotropic com pounds the most commonly employed being ^{131}I Rose Bengal The medium high photon energy and relatively long half life of this isotope requires that the adminis tered dose be kept low thereby causing a long scanning time with only a few scans obtainable during the first and most dynamic period of the examination

In this respect $^{99}Tc^{m}$ is to be preferred inasmuch as the amount of activity adminis tered can be high Furthermore the energy level of $^{99}Tc^{m}$ allows the use of a gamma camera Chelate binding of this isotope to suitable pharmaceutical compounds has been accomplished in recent years the two most commonly used agents being pyri doxilideneglutamate (PG) and 2 6-diethylacetanilideimino-diacetate (HIDA) Using these compounds it is possible to evaluate the excretion via the liver by rapid sequen tial images At the same time anatomic details above a certain size become demon strable among these the larger biliary ducts and the gallbladder The method cannot compete with radiography with contrast medium if this method can be employed Therefore the indication for scintigraphy will primarily include patients with an increase of serum bilirubin to a level exceeding twice the normal value and cases with hypersensitivity to radiographic contrast media in these cases hepatobiliary scinti graphy is a useful alternative

Unfortunately the abbreviation HIDA as used by different authors refers to the

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Table 1

*Characteristics of normal condition and criteria employed for classification of parenchymal disease and extrahepatic obstruction. * and ** cannot both be normal in the same case*

	Normal	Hepatocellular disease	Obstructive disease	Non-conclusive
Activity in liver				
Uptake	Maximum before 16 min post injection	Normal, delayed or reduced	Normal or delayed	Reduced relative to blood pool
Excretion	Almost total before 1 h post injection	Delayed but no retention at 24 h	Normal, delayed or none	None
Activity in biliary tract				
Accumulation	Demonstrable before 24 min post injection	Delayed or not demonstrable	*Normal, delayed or not demonstrable	None
Disappearance	Reduced at 1 h	No retention at 24 h	Delayed. Dilated biliary tract at any time or diffuse hepatic retention at 24 h	None
Activity in intestine	Demonstrable before 24 min post injection	Normal or delayed but demonstable at 24 h	**Normal, delayed or not demonstrable	None

Table 2

Relationship between scintigraphic diagnosis and definite diagnosis in the various groups

Scintigraphic diagnosis	Total series		Serum bilirubin 40 μmol/l or more		Serum bilirubin 40 to 250 μmol/l	
	Hepato-cellular disease	Ob-structive disease	Hepato-cellular disease	Ob-structive disease	Hepato-cellular disease	Ob-structive disease
Normal	3	9	1	1	1	1
Hepatocellular disease	14	6	13	2	12	2
Obstructive disease	3	23	2	20	2	18
Not conclusive	3	6	3	6	1	1
Total	23	44	19	29	16	22

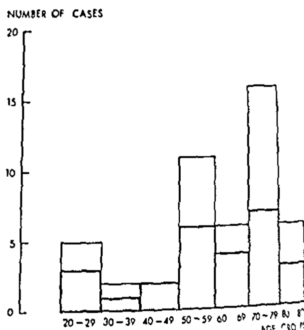


Fig 1 Age and sex distribution of the 48 patients with jaundice and serum bilirubin levels of 40 μmol/l or more White column = males Shaded column = females

methyl as well as the ethyl substitutions From a semantic point of view this may be correct but in clinical routine it is unpractical Although the ethyl substitution is preferred at present it is considered most suitable to let these names be synonymous

Material

The material comprised 6 normal subjects and 67 patients with either liver or biliary tract disease The mean age of the normal subjects was 38 years (range 31 to 49 years)

Of the 67 patients 51 had a serum bilirubin higher than 40 μmol/l at the time of examination The cause of jaundice could not be established in 3 cases the remaining 48 included 29 with extrahepatic obstruction and 19 with hepatocellular disease In 14 cases the diagnosis was obtained at surgery in 8 by liver biopsy and in 10 at post mortem examination The remaining 16 cases were considered to have been confirmed clinically by subsequent radiography or laboratory tests

The age and sex distribution of the 48 patients is given in Fig 1 The mean age was 61 years (range 20 to 84 years) 28 (58 per cent) were over 60 years of age

Methods

The examination was carried out with the patient in the supine position on the examination couch or in bed The gamma camera was placed with the collimator parallel to the anterior surface of the patient the centre pointing at the bisection of the right curvature and the right medio clavicular line The apparatus employed



Fig 3 Choledocholithiasis (confirmed at surgery) in a 58 year old male with a serum bilirubin level of 48 μmol l a) 1 h and b) 3½ h after injection Retention in the biliary tract Scintigraphic diagnosis Relative obstruction

respectively If no activity was found in the liver apart from that corresponding to the blood background and if evidence of biliary stasis or intestinal activity did not occur within 24 hours after injection it was concluded that the liver function was reduced Whether this reduction was caused by extrahepatic obstruction or hepato cellular disease could not be determined In these cases the result was classified as non-conclusive i e the examination produced no information as to the differential diagnosis

The following values were calculated in order to evaluate the accuracy of the method

Nosographic sensitivity The percentage of patients with a specific disease and with the characteristic scintigraphic findings

Nosographic specificity The percentage of patients without the disease and with out the characteristic scintigraphic findings

Diagnostic specificity The percentage of patients with the characteristic scinti graphic findings and with the specific disease

Diagnostic sensitivity The percentage of patients without the characteristic scinti graphic findings and without the specific disease

Differences between mean values were evaluated using the Wilcoxon test In percentage calculations figures within brackets refer to 95 per cent confidence limits

Results

The number of patients in the eight combination groups of scintigraphic diagnoses and diseases were registered in three matrices (Table 2) The first matrix includes the

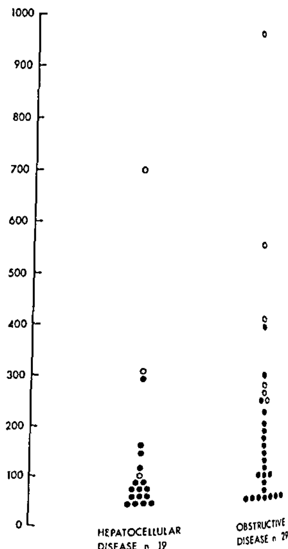


Fig 2 Serum bilirubin levels (μmol/l) for the individual 48 patients with hepatocellular disease and extrahepatic obstruction Star = Scintigraphically non conclusive

was either Nuclear Chicago s Pho gamma III Selektronik s Radicamera or General Electric s Maxicamera Parallel hole collimators were used except for the late recordings where whole body scanning equipment was often employed

Polaroid recording of oscilloscope images was commenced at the same time as 74 MBq (2 mCi) of $^{99}Tc^{m}$ HIDA (SOLCO-HIDA 10 mg) was injected intravenously Each recording covered a period of 4 min and the recording was continued for one hour Until tracer could be identified in the intestine late images were recorded at 3 6 and possibly 24 hours after injection

The recordings were evaluated without knowledge of the clinical diagnosis noting the following factors times of appearance and disappearance of activity in the liver and bile ducts width of the biliary tract and appearance time of activity in the duodenum

Table I lists the various characteristics of the normal series and the criteria employed for classification into hepatocellular disease and extrahepatic obstruction



Fig 4



Fig 5a



Fig 5b

Fig 4 Biliary tract carcinoma (surgically confirmed) in a 77 year old female with a serum bilirubin level of 387 μmol/l At 1 h after injection retention of activity in the gallbladder Scintigraphic diagnosis Obstruction

Fig 5 Choledocholithiasis and pancreatitis (surgically confirmed) in a 69 year old female with a serum bilirubin level of 90 μmol/l a) 1 h and b) 24 h after injection Considerable activity in the liver but no activity in the intestine Scintigraphic diagnosis Total obstruction

to the hospital and the examination In several cases this delay amounted to as much as one week The majority of patients were referred for a high serum bilirubin level which often had been normalized before the examination could be carried out In 2 patients one with hepatocellular disease serum bilirubin 58 μmol/l and one with extrahepatic obstruction serum bilirubin 49 μmol/l the scintigraphy was considered to be normal This may be due partly to a subjective estimate of the rate of build up of activity and partly to the diameter of the extrahepatic biliary tract

False abnormal scintigraphy In 3 patients with hepatocellular disease the scintigraphy was considered to indicate obstruction In the first case a patient with a serum bilirubin level of 58 μmol/l the explanation was an unusual position of the gallbladder which simulated dilatation of the extrahepatic biliary tract The second patient with liver metastases had a serum bilirubin value of 130 μmol/l and was classified as having hepatocellular disease However it is possible that the scintigraphic evaluation was actually correct and that the most important component in the genesis of jaundice was compression of the biliary tract The third patient had hepatic steatosis confirmed by biopsy with a serum bilirubin value of 9 μmol/l An intravenous cholangiography two years previously had demonstrated dilatation of the extrahepatic biliary tract but free passage to the duodenum

Six patients with extrahepatic obstruction had scintigraphic appearances consistent with hepatocellular disease In 4 cases with serum bilirubin levels of 23 27 31 and 143 μmol/l respectively the cause was assumed to be a temporary impediment due to the passage of a stone The scintigraphy was carried out at a time when clinical signs and laboratory tests indicated that the stone had passed to the duodenum The dilatation of the biliary tract was not of such magnitude as to be detectable on

Table 3

Diagnostic probability and nosographic frequency (per cent) of parenchymal disease and extrahepatic obstruction

	Total series	Serum bilirubin 40 μmol/l or more	Serum bilirubin 40 to 250 μmol/l
Hepatocellular disease			
Diagnostic specificity	70 (46–88)	87 (60–98)	86 (57 98)
Diagnostic sensitivity	81 (67–91)	82 (65–93)	83 (63 95)
Nosographic sensitivity	61 (39–80)	68 (43–87)	75 (48 93)
Nosographic specificity	86 (73–95)	93 (77–99)	91 (67 99)
Prevalence	34	40	4?
Obstructive disease			
Diagnostic specificity	88 (70 98)	91 (71–99)	90 (68 99)
Diagnostic sensitivity	49 (33 65)	65 (44–83)	78 (5? 94)
Nosographic sensitivity	52 (37–68)	69 (49–85)	82 (60–95)
Nosographic specificity	87 (66–97)	89 (67–99)	94 (70–100)
Prevalence	66	60	58

total series of 67 patients The second matrix comprises the 48 patients who complied with the criterion of a serum bilirubin level of 40 μmol/l or more and the third matrix the 38 patients who fulfilled the criterion of a serum bilirubin level between 40 and 250 μmol/l

The serum bilirubin level of each individual patient in the group of patients characterized by a serum bilirubin level of 40 μmol/l or more is given in Fig 2 The values ranged between 40 μmol/l and 700 μmol/l for the patients in the group with hepatocellular disease the mean value was 128 μmol/l and the median 65 μmol/l In the group with extrahepatic obstruction the lowest value was 43 μmol/l and the highest 963 μmol/l the mean value was 184 μmol/l and the median 107 μmol/l These mean values are not significantly different

In 9 of 33 patients (19 %) the result of scintigraphy was non conclusive (Fig 2) In this group the lowest serum bilirubin value was 91 μmol/l and the highest 963 μmol/l In 7 cases the serum bilirubin level was higher than 250 μmol/l

It is evident from Table 2 and Fig 2 that limiting the series to include only patients with serum bilirubin values between 40 and 250 μmol/l would reduce the number to 38 The distribution of the 10 patients thus excluded would be 3 with hepatocellular disease and 7 with extrahepatic obstruction in 7 of these 10 scintigraphy was non-conclusive

A survey of nosographic and diagnostic specificity and sensitivity within the groups appears in Table 3 Figs 3 to 8 exemplify scintigraphic findings

False normal scintigraphy One reason why a normal scintigraphy may be obtained from a patient with jaundice is the time interval between the referral of the patient

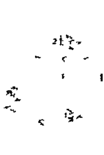


Fig 7a

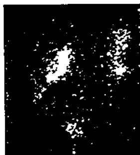


Fig 7b



Fig 8

Fig 7 Liver metastases (surgically confirmed) in a 62 year-old male with a serum bilirubin level of 130 μmol/l a) 1 h and b) 24 h after injection Retained activity in the dilated biliary tract Scintigraphic diagnosis Relative obstruction (erroneous abnormal diagnosis)

Fig 8 Choledocholithiasis (surgically confirmed) in a 72 year-old male with a serum bilirubin level of 27 μmol/l At 1 h after injection delayed excretion to the intestine but no stasis Scintigraphic diagnosis Parenchymal disease (erroneous abnormal diagnosis)

regarded it may be substantial under pathologic conditions Further experiments showed that the substitution of methyl by ethyl lowered the urinary excretion from 15 to 5 per cent in the first hour (WISTOW et coll 1977) The new compound ^{99}Tc^{m} 2 6 diethylacetanilideiminodiacetic acid at present appears to be the most promising ^{99}Tc^{m} labelled hepatobiliary agent although the low renal excretion rate of ^{131}I Rose Bengal has not yet been reached

Only very little experience from the use of this new compound in man has been published mainly in the form of abstracts (BIERSACK et coll 1977 COX et coll 1977 NIELSEN et coll 1977 SAUER & ADLER 1977 WELCKE et coll 1977) The information available is not particularly detailed and does not permit any reliable conclusions regarding the diagnostic value of the examination

MATOLO et coll (1976) employed ^{99}Tc^{m} PG in 10 normal subjects and 19 patients with jaundice ^{99}Tc^{m} PG is presumed to have characteristics corresponding to those of ^{99}Tc^{m} HIDA In all the normal subjects the liver was demonstrated 5 min after administration of the tracer the extrahepatic biliary tract gallbladder and duodenum approximately 10 min later The patients with jaundice had serum bilirubin levels between 2 1 and 23 3 mg/100 ml (36–400 μmol/l) and in all cases the scintigraphic differentiation between hepatocellular disease and extrahepatic obstruction was possible using 74 MBq (2 mCi) for the normal subjects and 150 to 185 MBq (4–5 mCi) for the patients with jaundice The following year (1977) MATOLO et coll published further experiences from 27 normal subjects and 55 patients with jaundice The results from the first series were reproduced employing the same method and with serum bilirubin values of up to 927 μmol/l

In normal subjects the present results agree well with those published by others while the differential diagnostic sensitivity is lower in the present series The diagnostic

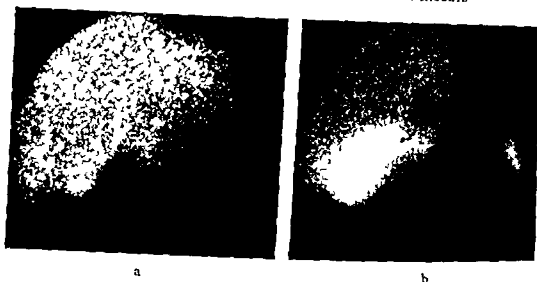


Fig 6 Liver cirrhosis (surgically confirmed) in a 27 year old male with a serum bilirubin level of 60 µmol/l a) 12–16 min and b) 1 h after injection Only slight uptake of activity in the liver but normal excretion Scintigraphic diagnosis Parenchymal disease

the gamma camera image Thus it was only possible to demonstrate the reduced function of the liver parenchyma In all 4 cases stones were later demonstrated in the gallbladder One further patient with a serum bilirubin value of 24 µmol/l had a multifocal cholangiocellular carcinoma and possibly the definition of extrahepatic obstruction may have contributed to an erroneous evaluation in this case The sixth patient had a carcinoma of the head of the pancreas, and a serum bilirubin value of only 46 µmol/l

Non conclusive scintigraphy The fact that scintigraphy does not yield diagnostic information may sometimes be attributed to reduced liver function to such an extent that the amount of activity excreted does not for statistic reasons permit reliable differentiation of the liver from the blood background Such non conclusive results will be encountered in patients with a severe reduction in liver function and a high serum bilirubin level irrespective of the cause Nevertheless, one of the non conclusive scintigraphic examinations occurred in a patient with hepatocellular disease due to a longstanding and severe liver cirrhosis with a serum bilirubin value of 91 µmol/l

Discussion

In 1975 HARVEY et coll described the synthesis of $^{99}Tc^{m}$ 2 6 dimethylacetanilid deiminodiacetic acid and the first animal experiments were carried out by LOBERG et coll (1976) In dogs only 3 per cent of the amount of activity administered was found in the blood half an hour after the injection 82 to 87 per cent of the compound being eliminated via the liver and the remainder through the kidneys Although the renal excretion under normal circumstances can for all practical purposes be dis-

disease The reason for this may be either that parenchymal disease is actually present or that an obstruction although no longer present has left a *residual depression of* parenchymal function

Several methods have been developed in recent years for the diagnosis of jaundice first and foremost endoscopic retrograde cholangiopancreatography (ERCP) and *percutaneous transhepatic cholangiography* (PTC) It is impossible on the basis of the present results to predict to what extent scintigraphy will replace or supplement these methods If further experience confirms that scintigraphy is less suitable with serum bilirubin levels higher than 250 μmol/l then patients with a level above this will constitute primary candidates for ERCP and PTC

On the other hand in patients with serum bilirubin levels below 250 μmol/l scintigraphy with $^{99}Tc^m$ HIDA is a differential diagnostic examination with a reasonable specificity and sensitivity The important advantages of scintigraphy as compared with ERCP and PTC should also be kept in mind scintigraphy causes little discomfort to the patient it may conveniently be repeated later in the disease it has no contra indications and no morbidity or mortality However in cases of partial or total extrahepatic obstruction scintigraphy in all probability will only indicate that the genesis of the jaundice is obstruction without details regarding its cause—information that will often be available with ERCP or PTC

A final definition of the limits for the use of scintigraphy must be based on further comparison between the relative merits of scintigraphy ERCP and PTC

SUMMARY

In order to assess the clinical value of $^{99}Tc^m$ HIDA for hepatobiliary scintigraphy 23 patients with hepatocellular disease and 44 patients with obstructive biliary tract disease were examined Positive information was obtained in 14 and 23 patients respectively False results mainly depended *on inadequate imaging of the liver in the case of severely impaired* function whatever the cause Spontaneously ameliorated obstruction leaving an impaired hepatocellular function may give misleading results A malignant tumour widely involving the liver and impressing the bile ducts may also create the appearance of obstruction If HIDA scintigraphy be limited to patients with serum bilirubin levels between 40 and 250 μmol l the diagnostic specificity and sensitivity of 90 per cent and 78 per cent respectively is reached in demonstrating obstruction when the prevalence is 0 58

ZUSAMMENFASSUNG

Um den klinischen Wert von $^{99}Tc^m$ *HIDA fur die Leber Gallen Szintigraphie festzustellen* wurden 23 Patienten mit hepatozellularer Erkrankung und 44 Patienten mit einer obstruktiven Erkrankung des Gallenganges untersucht Positive Information wurde bei 14 bzw 23 Patienten erhalten Falsche Resultate beruhten hauptsachlich auf einer fehlerhaften Darstellung der Leber bei Fallen mit einer schwer veranderten Funktion unabhangig von der Ursache Eine spontan aufgehobene Obstruktion die eine *verbesserte hepatozellulare* Funktion zur Folge hat kann fehlerhafte Resultate geben Ein maligner Tumor der die Leber weit umfasst und *auf die Gallengange* druckt kann auch das Bild einer Obstruktion

value of the method is expressed both as diagnostic and nosographic specificity and sensitivity The diagnostic probability achieved is the decisive factor with regard to the usefulness of the method However, these factors are dependent on the prevalence as well as the nosographic frequency in cases of hepatocellular disease and extrahepatic obstruction As conditions may vary from department to department it was decided to include the nosographic frequency as well If the calculations are carried out on the patient material in matrix No 2 of Table 2, the diagnostic specificity and sensitivity of the diagnosis extrahepatic obstruction will be 91 per cent (71-99) and 65 per cent (44-83) respectively The corresponding values for the diagnosis hepatocellular disease are 87 per cent (60-98) and 82 per cent (65-93) respectively It may be said for both diagnoses that the specificity is reasonably good, but that the sensitivity for the diagnosis extrahepatic obstruction is unacceptably low It is obvious that the reason is the relatively large number of non conclusive results This is the case in 9 of the 48 patients (19 %) It is clear that there is a relationship between the serum bilirubin level and the ability of the method to provide a clear conclusion Seven of the 9 patients had a serum bilirubin value higher than 250 μmol/l The highest value where the examination was diagnostically useful was 387 μmol/l and this was found in a patient with extrahepatic obstruction MATOLO et coll (1977) obtained a conclusive diagnosis with considerably higher bilirubin values However it is not possible to ascertain from the report how many cases had a serum bilirubin value higher than 250 μmol/l Values exceeding this limit in the present series contributed substantially to the difficulty in reaching a conclusive scintigraphy

On the basis of the present experiences hepatobiliary scintigraphy with $^{99}Tc^m$ HIDA appears to be most useful with serum bilirubin levels between 40 and 250 μmol/l Only in 2 (3 %) of the 38 patients in this group (matrix No 3 Table 2) did the scintigraphy provide insufficient information for the differential diagnosis Under such conditions the diagnostic specificity and sensitivity for the diagnosis of extrahepatic obstruction were 90 per cent (68–99) and 78 per cent (52–94) respectively The corresponding values for the diagnosis hepatocellular disease were 86 per cent (57–98) and 83 per cent (63–95)

Patients were not included in the series on a consecutive basis The reason for this was not deliberate selection of certain patient categories but a limited scintigraphic capacity For the most part the scintigraphy could be carried out on one certain day of the week only Because of this a waiting period extending to a full week in the most unfortunate cases could occur which meant that several patients developed serum bilirubin values higher than 250 μmol/l This impaired the diagnostic value of the examination With better capacity it may be possible to examine all patients with jaundice shortly after admission at a time when relatively fewer patients will have a high serum bilirubin level thus improving the diagnostic value of the scintigraphy

Furthermore scintigraphy of the biliary tract of patients during the phase when the serum bilirubin level decreases after a maximum will often simulate parenchymal

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ANGIOGRAPHY AND SCINTIGRAPHY IN PATIENTS WITH POSSIBLE LIVER MALIGNANCY

C HELLEKANT and E CEDERQVIST

In the staging of malignant disease and planning of the therapy in liver malignancy exclusion or demonstration of metastases to the liver and in the latter case demonstration of their extent is of great importance Physical examination is unreliable as a liver of normal size is found in 30 to 54 per cent of patients with proven liver metastases (OZARDA & PICKREN 1962 POULOSE et coll 1969) on the other hand an enlarged liver may be caused by cirrhosis hepatitis or cystic disease The same authors also state that about 15 per cent of hepatic metastases are missed at palpation during operation due to their position

Although sensitive liver function tests lack specificity and can only raise a suggestion of malignancy (SCHAEFFER & SCHIFF 1965 POULOSE et coll) Blind percutaneous aspiration needle biopsy of the liver gives correct positive diagnosis in 77 per cent but also 20 per cent false negative diagnoses (LUNDQUIST 1971)

Angiography and scintigraphy of the liver have a high diagnostic yield but both methods also give false positive and negative diagnoses

The value and limitations of these two methods were analyzed in 100 patients with suggested liver malignancy as well as possible reasons for an incorrect diagnosis in each case The results are now reported

Material and Methods

The material consisted of 100 patients Angiography and scintigraphy were performed within 4 weeks in all cases but usually with a shorter interval The written

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hervorrufen Falls die HIDA Szintigraphie auf Patienten mit Serum Bilirubin Spiegeln zwischen 40 und 250 μmol/l eingeschrankt wird wird eine diagnostische Spezifitat und Empfindlichkeit von 90 bis 78 Prozent zum Nachweis einer Obstruktion erreicht wenn ein Übergewicht von 0 58 vorliegt

RÉSUME

Pour déterminer l intérêt clinique du $^{99}Tc^{m}$ HIDA pour la scintigraphie hépatobiliaire 23 malades atteints d affection hépatocellulaire et 44 malades ayant une affection obstructive des voies biliaires ont été examinés Des informations positives ont été obtenues chez respectivement 14 et 23 malades Les faux resultats ont dépendu principalement d une image inadéquate du foie dans le cas ou la fonction hépatique était gravement atteinte quelle qu en fut la cause Une obstruction s améliorant spontanément en laissant une détérioration de la fonction hépatocellulaire peut donner un résultat trompeur Une tumeur maligne atteignant largement le foie et comprimant les voies biliaires peut aussi créer l aspect d une obstruction Si la scintigraphie avec l HIDA est limitée aux malades qui ont des taux de bilirubine sérique compris entre 40 et 250 μmol/l on atteint dans la mise en évidence d une obstruction une spécificité diagnostique de 90% et une sensibilité de 78% quand la prevalence est de 0 58

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Angiography and scintigraphy of the liver have a high diagnostic yield but both methods also give false positive and negative diagnoses

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Material and Methods

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reports given in connection with the examination were compared with data from the patients files

The angiographic reports usually contained a conclusion concerning presence or absence of liver malignancy The scans were reported as pathologic probably pathologic or normal A description of the distribution of the isotope was also given Often a compatible diagnosis was suggested such as expansive lesion or 'metastases

All reports classified as pathologic or probably pathologic with local defects or strongly irregular uptake were registered as positive

Malignancy was proven with laparotomy needle biopsy autopsy or combinations of these

The liver was considered free from malignancy if laparotomy with biopsy had been negative In 12 cases only needle biopsy with negative result was performed All these patients were retrieved and lived without signs of liver neoplasm at least one year after the actual angiography or liver scintigraphy

All angiographies and scans where the original reports did not coincide with the final diagnoses were reviewed and possible reasons for this evaluated

The material included 8 patients with primary hepatoma 6 with carcinoma of the bile ducts or gallbladder and 37 with liver metastases from other tumors Among the 49 patients without liver malignancy 14 had obstructive jaundice of different severity 3 hepatitis 5 slight fatty infiltration 3 moderate cirrhosis 3 cystic liver disease and one a suggested but not confirmed hemangioma

In 20 patients no evidence of liver disease was found

Angiography was performed with percutaneous catheterization of the femoral artery and the tip of the catheter was placed in the celiac or the superior mesenteric artery depending on the anatomy In most cases a simultaneous celiac and superior mesenteric angiography was carried out with injection of 40 ml of Isopaque 280 (Nyegaard Norway) at a rate of 12 to 15 ml per second Films were taken in a p and right posterior oblique projections at a speed of one film per s for 2 s 2 films per s for 5 s and then one film every other second for 8 s covering a total of 15 seconds In 58 patients also a selective angiography of the hepatic artery was performed with 20 to 30 ml of contrast medium injected at a rate of 8 to 10 ml per second In 50 patients an additional angiography was performed with infusion technique using 50 ml of contrast medium at a rate of 5 ml per s and films taken every other second for 32 seconds

Scintigraphy Most of the examinations were performed with a rectilinear scintigraph equipped with a 5 inch × 2 inch (12 7 cm × 5 08 cm) NaI (Tl) scintillation detector and presented as full size colour and photoscans In a few cases a gamma camera was used Two mCi $^{99}Tc^{m}$ sulphur colloid were administered Anterior and right lateral scans were performed with the patient supine and on his left side

Table

Relation between angiographic and scintigraphic reports in 100 patients with suggested liver malignancy

Scintigraphy	Angiography			Total
	Correct	False pos	False neg	
Correct	70	5	4	79
False pos	12	5	—	17
False neg	1	—	3	4
Total	83	10	7	100

Results

The results are summarized in the Table

Angiography The prospective diagnosis concerning liver malignancy was correct in 83 patients false positive in 10 and false negative in 7 patients Of these 5 and 4 respectively were correctly evaluated in the scan reports

Scintigraphy The scan was correctly interpreted in 79 patients false positive in 17 and false negative in 4 patients Of these 12 and one respectively were correctly evaluated in the angiographic report

Angiography and scintigraphy Both methods gave false positive results in 5 patients and false negative diagnoses in 3 patients

At review 2 of the false positive and 2 of the false negative angiographies as well as 8 of the false positive scans were believed to be caused by lack of experience at the primary evaluation The 5 cases with both false positive angiography and scintigraphy could be reduced to one by comparing the examinations The number of combined false negative diagnoses was unchanged

Analyses of the cases

False positive angiography—correct scintigraphy (5 patients) Local or general irregular accumulation of contrast medium in the liver parenchyma caused the false positive diagnoses in 2 patients where the angiography included a series with slow injection of a large amount of medium in the hepatic artery and the celiac trunk respectively One of the patients had a normal right lobe after previous resection of the left lobe cause of bile duct carcinoma The other had obstructive jaundice A review of these films revealed that the irregular accumulation could be explained by filling of branches of the portal or hepatic veins Wide bile ducts also may have been responsible in the patient with jaundice

Vascular injury and displacement after previous diagnostic punctures contributed to the diagnostic difficulties in another patient with obstructive jaundice

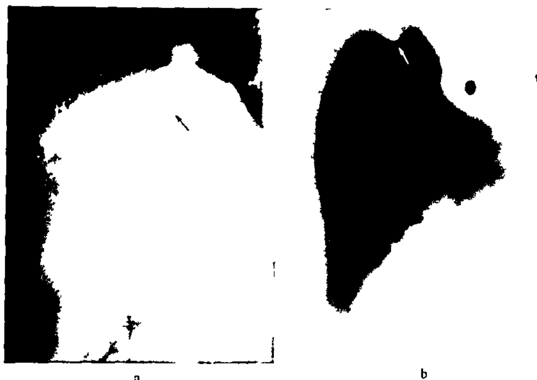


Fig 1 a) Parenchymal phase of hepatic angiography after 1 µg hypertensin in the hepatic artery Accumulation of contrast medium within a rounded area (→) primarily considered as metastases At review it was recognized as a hemangioma b) $^{99}Tc^{m}$ sulphur colloid scan Small defect cranially in the right lobe (→)

Tortuous or irregular arterial branches suggested tumor infiltration in one case with siderosis and fibrosis and in another with a slight fatty infiltration In the first case the impression of malignancy was enhanced by an a p shunt in connection with the vascular irregularities without preceding puncture

False negative angiography—correct scintigraphy (4 patients) In 2 patients the review also failed to indicate liver malignancy One of the examinations revealed a pancreatic carcinoma but gave no evidence of numerous liver metastases demonstrated at the scintigraphy

The other had a large central bile duct carcinoma demonstrated at a later percutaneous transhepatic cholangiography In the other 2 patients displaced arteries and rounded areas with more or less accumulation of contrast medium than the surrounding parenchyma should have suggested metastases These patients had multiple metastases from esophageal and cecal carcinoma respectively and the lesions were clearly observed on the scans

The erroneous evaluation of the angiographic films could partly be explained by a slight underexposure in one case and a too slow injection of contrast medium in the other


a


b


c

Fig 2 a) Arterial phase of celiac angiography in patient with no liver malignancy The vessels appear stretched around large avascular mass medially in the right lobe (↔) Distended gallbladder (→) b) Parenchymal phase of hepatic angiography with infusion technique Seemingly compressed parenchyma around avascular area (→) c) Angiography of the superior mesenteric artery Aberrant artery supplying the actual part of the liver

False positive scintigraphy—correct angiography (12 patients) Irregular uptake or local defects suggested liver malignancy in these patients Among 6 patients with normal livers 3 had a locally decreased uptake at the liver hilum and impression from the costal arch respectively

In another patient a thin left hepatic lobe probably was the cause of low activity in the a p projection All these 4 scans were in retrospect recognized as normal variations



Fig 3 Same case as in Fig 2 Scintigraphy Defects (→) in upper and lower margins of the right lobe Comparison to the angiography confirmed that the defects were caused by a large heart and a dilated gallbladder respectively

In 2 patients with Hodgkin s disease a generally irregular uptake of the isotope erroneously suggested infiltration of the liver and this was also the case with 6 patients with jaundice The impression was enhanced in one of these by a lateral well circumscribed defect caused by an extrahepatic abscess demonstrated at angiography and in another by blurring of the liver margins due to respiratory motion

In 2 patients with severe obstructive jaundice rounded local defects appeared in the scan Percutaneous transhepatic cholangiography had been performed within a week before scintigraphy and in one of the patients a draining catheter was left in the liver The defects were evaluated as indicating metastases but may have been small hematomas after the puntcures and wide bile ducts

False negative scintigraphy—correct angiography (one patient) Angiography demonstrated a couple of 4 cm large metastases in the right lobe of the liver in a patient with a rectal carcinoma while the scan also at the review was considered as normal The reason for this error is not known

False positive diagnosis by both methods (5 patients) In one of them a lesion was diagnosed at the primary angiography as a probable metastasis but considered to be a hemangioma at review of the films The scan showed a defect at the same location and the clinical history suggested malignancy (Fig 1) In spite of several biopsies during laparotomy no metastases or other abnormality were found at repeat angiography and scintigraphy 9 months later no abnormality was demonstrated

In the other 4 patients no clinical evidence of liver disease was found In a patient with Hodgkin s disease both methods demonstrated a patchy appearance of the parenchyma within the capillary phase which was considered as a strong indication of liver involvement At the review of the angiography it was noted that the splenic vein was compressed in the neighbourhood of the pancreas and that no filling of the intrahepatic portal vein had occurred Instead a dense filling of the hepatic veins was seen indicating a rapid arterio venous shunting due to impaired portal circulation This may also have caused the irregular uptake of the isotope At laparotomy



Fig 4 Hepatic angiography one week after needle biopsy of the liver Stretched arteries in the upper part of the right lobe suggesting tumor (→) At the review an occluded artery (↔) was recognized indicating a hematoma

with splenectomy no parenchymal involvement was found but there were several large lymph nodes around the celiac root compressing the splenic vein

In one patient celiac and selective hepatic angiography demonstrated a 6 cm large rounded avascular area medially in the right lobe suggesting an expanding lesion The vessels surrounding the area also appeared to be displaced (Fig 2 a b) An additional angiography demonstrated an abberant artery from the superior mesenteric artery supplying the actual part of the liver (Fig 2 c)

The scan also demonstrated local defects one in the upper margin of the right lobe the other corresponding to the gallbladder fossa Comparison to the angiography confirmed that the defects were caused by a large heart and a dilated gall bladder respectively (Fig 3)

In another patient stretched arteries in the medial part of the right lobe and irregular accumulation of contrast medium suggested malignancy However at the review an occluded artery leading to this area was recognized indicating a hematoma from a needle puncture performed one week earlier (Fig 4)

The defects at the scan were located marginally probably representing respiratory motion another defect corresponded to the angiographic finding

In the last patient an irregular accumulation during infusion angiography was considered as representing metastases while a locally decreased uptake at the scan



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Fig 4 Hepatic angiography one week after needle biopsy of the liver Stretched arteries in the upper part of the right lobe suggesting tumor (→) At the review an occluded artery (↔) was recognized indicating a hematoma

with splenectomy no parenchymal involvement was found but there were several large lymph nodes around the celiac root compressing the splenic vein

In one patient celiac and selective hepatic angiography demonstrated a 6 cm large rounded avascular area medially in the right lobe suggesting an expanding lesion The vessels surrounding the area also appeared to be displaced (Fig 2 a b) An additional angiography demonstrated an abberant artery from the superior mesenteric artery supplying the actual part of the liver (Fig 2 c)

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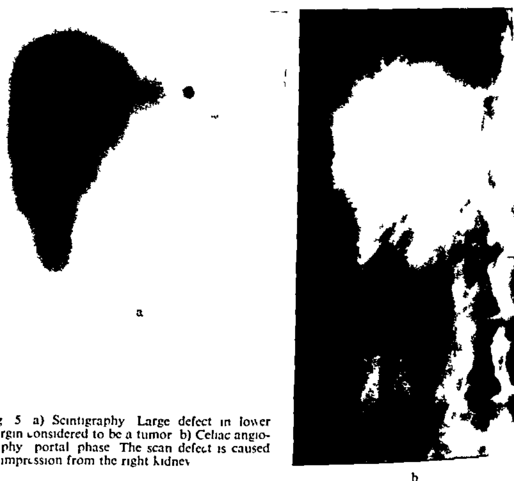


Fig 5 a) Scintigraphy Large defect in lower margin considered to be a tumor b) Celiac angiography portal phase The scan defect is caused by impression from the right kidney

when compared to the angiography turned out to be caused by the right kidne (Fig 5)

False negative diagnosis by both methods (3 patients) One of these had a larg pancreatic carcinoma Both methods demonstrated the tumor but not that it invade the liver

The other 2 patients had very small malignant lesions One had metastases on th liver surface less than one cm in diameter from a colon carcinoma the other sma Hodgkin s infiltrates throughout the liver

Discussion

Neither angiography nor scintigraphy is specific in detecting tumors but both ma indicate malignancy (REUTER & REDMAN 1972 OSTER et coll 1975)

At angiography the ability to detect a liver tumor mainly depends on its vasculari relative to the parenchyma surrounding it Richly vascularized tumors are easil demonstrated down to a size less than one cm and hypovascular tumors as small a

to 3 cm may appear as filling defects On the other hand many metastases appear to have the same vascularity as the surrounding parenchyma and therefore are difficult to detect This is also true for many cholangiocarcinomas (KAUDE & RIAN 1971)

At scintigraphy the lesions appear as areas with diminished or absent activity due to paucity or hypofunction of the reticuloendothelial cells The main limiting factors are respiratory motion the thickness of the liver parenchyma and the size and location of the lesion According to MCAFFE et coll (1965) space occupying lesions larger than 2 5 cm usually can be detected while COVINGTON (1970 a) and CONN (1972) state that all lesions less than 3 cm in diameter are missed regardless of their position in the liver This is a serious drawback since it has been reported that 31 per cent of patients with hepatic tumors at autopsy have a maximum tumor diameter less than 2 cm (OZARDA & PICKREN 1962)

The reported over all accuracy of scintigraphy in detecting presence or absence of liver disease varies between 75 per cent (WANG et coll 1971) and 90 per cent (FERRANTE & MAXFIELD 1968) Corresponding figures for angiography are in the same range (NEBESAR et coll 1966 ROSSI & GOULD 1970 WANG et coll) but the figures for space occupying lesions are even higher (NEBESAR et coll 1966 ROSSI & GOULD WANG et coll DU PRIEST et coll 1973)

The major problem in liver scintigraphy seems to be the high number of false positive diagnoses while the false negative seems to be a minor one DU PRIEST et coll used scintigraphy as a screening test and identified 14 of 15 patients with liver metastases but also had 47 5 per cent false positive diagnoses ALMERSJÖ et coll (1974) also had 40 per cent false positive diagnoses in a material of 198 patients but no false negative

Causes for false positive diagnosis at liver scintigraphy are listed by FREEMAN et coll (1969) and COVINGTON (1970 b) and include normal anatomic structures such as the gallbladder fossa the porta hepatis a thinned out or small left lobe of the liver extrinsic defects of ribs vertebrae or kidney and peculiar shapes of the liver but also pressure from tumors in adjacent organs Lacking experience also tends to give a higher incidence especially of false positive diagnoses (NISHIYAMA et coll 1975)

The present material included 49 patients with no evidence of liver malignancy The scan was wrongly interpreted as positive in 17 of these At the review 8 of the erroneous diagnoses could be referred to lacking experience by the primary examiner and in several of these the angiography clearly demonstrated the underlying anatomy Of the remaining 9 scans one had a local defect corresponding to a lesion at the primary angiography erroneously considered as metastasis and at the review of the films as a hemangioma which however was not confirmed the other 8 had a diffuse irregular uptake of the isotope Such irregularity may be caused by multiple metastases but also by other disorders such as cirrhosis or hepatitis especially if combined with jaundice In addition obstructive jaundice with wide bile ducts may simulate rounded metastases However in patients with cirrhosis the distribution of the iso-

tope in the bone marrow and spleen is often typical Five of the patients in this group had jaundice and 3 had Hodgkin s disease without proved liver involvement.

According to LITTON et coll (1972) and LANDBERG et coll (1974) only focal defects should be considered as a strong indication of liver involvement in the staging of patients with Hodgkin s disease while a diffuse irregular uptake of the isotope not warrants the diagnosis

The causes for false positive angiographies are not thoroughly discussed in the literature

In 4 of the present cases an irregular accumulation of contrast medium in the liver parenchyma was the major reason for a false positive diagnosis Such an irregular accumulation could be caused by multiple small metastases but also by regeneration nodules in cirrhosis or wide bile ducts in jaundice and should be evaluated with care, particularly if an infusion angiography has been performed with filling of the hepatic veins which often enhances the impression of irregularity JENSEN et coll 1973)

Stretched arteries partly caused the false positive diagnosis in 3 patients Such displacement may be due to tumor growth but if seen only locally and especially in the periphery of the liver or combined with a single arterio portal shunt may be caused by a recent diagnostic puncture (HELLEKANT 1976)

Arterio portal shunting is also often observed in patients with cirrhosis or after trauma and should not be considered as indicating malignancy unless in connection with a richly vascularized tumor usually then a hepatoma

According to the literature false negative results are a much smaller problem especially if both methods are used KIM et coll (1975) identified liver malignancy with angiography or scintigraphy in 97 per cent of 118 patients This is in accordance with the experiences at these hospitals Among 51 patients 11 examinations were erroneously reported as negative 7 with angiography and 4 with scintigraphy However in only 3 cases both methods failed 2 had very small tumor infiltrates and one a pancreatic carcinoma growing into the liver hilum In the other 8 patients the malignancy was diagnosed either with scintigraphy or angiography Only in one patient angiography revealed metastases not demonstrated at scintigraphy

With development of gray scale ultrasound and computer tomography new tools have become available in liver imaging The ability of ultrasound to differentiate between cysts abscesses and tumors which produce non specific cold areas in the scans makes it suitable as a complementary modality It may also help to differentiate defects due to anatomic variation from significant pathology (TAYLOR et coll 1977) and thereby decrease the number of false positive diagnoses

The accuracy of computer tomography in detecting primary and secondary hepatic tumors has not yet been established but preliminary results indicate that it is equal to scintigraphy (ALFIDI et coll 1976)

Conclusion

Scintigraphy should always precede angiography in patients with suggested liver malignancy A normal scan does not exclude liver malignancy but if such a lesion is present, it is usually too small to give signs or symptoms and may not be diagnosed even at laparotomy The scintigraphy should be repeated as soon as clinical data suggest metastases

A scan typical for metastases should be followed by a diagnostic fine needle biopsy and does not justify angiography unless the needle biopsy is negative or knowledge of the anatomy is needed before surgery or local intra arterial chemotherapy Angiography should always be performed with high demands of quality and a thorough knowledge of normal anatomy and different angiographic appearances A probably abnormal scan or angiography should be evaluated with care bearing in mind the high percentage of erroneous positive diagnoses By comparing an abnormal or probably abnormal scan with available films many mistakes can be avoided

SUMMARY

Angiography and $^{99}Tc^m$ scintigraphy were performed in 100 adult patients with suggested primary or secondary liver malignancy The results were compared to the final diagnosis obtained by biopsy surgery autopsy or long term clinical follow up The reasons for false positive and negative diagnoses are discussed in detail

ZUSAMMENFASSUNG

Angiographie und $^{99}Tc^m$ Szintigraphie wurden bei 100 erwachsenen Patienten bei denen eine primare und sekundare Lebermalignitat vermutet war durchgefuhrt Die Ergebnisse wurden mit der endgultigen Diagnose die durch Biopsie Chirurgie Autopsie oder durch langzeitige klinische Observation erhalten war verglichen Die Ursache fur falsche positive und negative Diagnosen werden im einzeln diskutiert

RÉSUME

Cent malades adultes suspects d avoir une tumeur maligne hepatique primitive ou secondaire ont éte examinés par angiographie et par scintigraphie au $^{99}Tc^m$ Les resultats ont éte comparés au diagnostic final obtenu par biopsie operation autopsie ou surveillance clinique prolongee Les auteurs examinent les raisons des diagnostics faussement positifs et faussement negatifs

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PALLIATIVE EMBOLIZATION OF ARTERIAL RENAL TUMOUR SUPPLY

Results in 10 cases

L EKELUND W MÅNSSON A M OLSSON and L STIGSSON

Transcatheter occlusion of the arterial supply of renal tumours is receiving increasing clinical interest (ALMGÅRD et coll 1973 BEN MENACHEM et coll 1975 BUCHELER et coll 1976 GOLDSTEIN et coll 1976 ALMGÅRD & SLEZAK 1977 GIULIANI et coll 1977 BERGREEN et coll 1977) This technique may be applied either preoperatively to facilitate nephrectomy or as a procedure in order to attempt palliation of local tumour symptoms in patients who for one reason or another are not considered for surgery While clinical experience with this technique is increasing an evaluation of its therapeutic value is important Therefore the results following embolization of renal tumour arterial supply in 10 patients are now reported

Material and Methods

The material comprised 10 patients 4 females and 6 males aged between 48 and 81 years Macroscopic hematuria was the presenting symptom in 4 patients while metastases were primarily detected in 3 Two patients were examined because of flank pain one of these had polycystic disease with a carcinoma in the left kidney Embolization in this particular case was performed preoperatively in an attempt to correct a severe hypercalcemia which was considered to be secondary to the renal

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carcinoma Six of the patients had pulmonary metastases at the time of emboliza tion, one had skeletal metastases and one liver metastases, why nephrectomy was not considered One 81 year old female with a large tumour of the right kidney was not considered for surgery because of age and cardiac problems

In 6 of the patients Bucrylate (isobuthyl 2 cyanoacrylate Ethichon Germany) was used for the occlusion of the renal artery One of these had 2 arteries feeding the tumour and autologous muscle tissue was injected into one of the arteries The Bucrylate was injected through a small teflon catheter introduced coaxially through the catheter in the renal artery The coaxial catheter was flushed with dextrose 5% in water solution in order to prevent occlusion following Bucrylate injection The amount of Bucrylate varied but more than 0 5 ml was not injected at one time In the remaining 4 patients small pieces of Spongostan (Ferrosan Sweden 99% gela tin—similar to gelfoam) was used as the embolic material in 2 of the patients together with the deposition of metallic coils in the renal artery in order to obtain a permanent occlusion These coils are provided in the Gianturco arterial occluder set (Cook Inc USA)

In one patient (Case 2) emergency nephrectomy was carried out because of severe flank pain following the embolization in the remaining 9 patients no nephrectomy was performed Three of the patients received progesterone therapy as well

In 8 of the patients embolization was performed as a separate procedure and not in direct connection with diagnostic angiography In 7 patients repeat angiography at various intervals after embolization was performed in order to evaluate the effect of the occlusion In one patient the size of the embolized kidney was followed by repeat ultrasound examinations All patients have been closely followed clinically including repeat chest radiography Four of the patients died and autopsy was performed in 3

Results

The results of the embolization appear in the Table Six patients are alive 3 3 3 14 18 and 24 months after embolization respectively Three of these had pulmonary metastases at the time of embolization and one had skeletal metastases

A 58 year old man (Case 8) with hemiparesis aphasia pulmonary metastases and at brain scintigraphy a lesion in the parietal lobe on the left side had a mass in the left kidney which at angiography was found to be a carcinoma (Fig 1 a) Because of the existence of metastases no surgery was considered and the tumour was occluded by transcatheter embolization with Bucrylate (Fig 1 b) Progesterone therapy was instituted as well, and chest films 4 months later demonstrated regression of the pulmonary metastases Repeat angiography was performed 8 months following em bolization and the left renal artery was found to be still occluded At 18 months following embolization chest films were normal and the patient was doing well Repeat scintigraphy of the brain was also without evident abnormality

One 48 year old man (Case 9) with general signs of malignancy including elevated

Table

Results of embolization of the renal artery in 10 patients

Case	Age	Sex	Metastases	Embolic material	Follow up
1	60	M	Liver	Muscle tissue + Bucrylate (2 renal arteries)	Reflux of embolic material with occlusion of right external iliac artery Operated with embolectomy but general deterioration with anuria Died 10 days after embolization
2	55	F	—	Spongostan	Nephrectomy same day as embolization because of severe pain Alive with pulmonary metastases 24 months after nephrectomy
3	68	M	Multiple pulmonary	Bucrylate (2 renal arteries both occluded)	Hematuria disappeared Died 8 months after embolization No autopsy
4	57	M	Multiple pulmonary	Bucrylate Reembolized twice	Hematuria disappeared initially 1 month control angiography partial revascularization Reembolization Recurring hematuria Angiography 7 months after initial embolization recanalization why reembolization was undertaken Died 5 months later Autopsy carcinoma in horse shoe kidney Extensive metastases Renal artery still occluded
5	67	F	Multiple pulmonary	Bucrylate	Pelvic carcinoma Hematuria disappeared Angiography 2 months after embolization persistent occlusion Died 3 months after embolization Autopsy extensive metastases Renal artery occluded Infarcted kidney but vital malignant cells in places
6	66	F	Multiple pulmonary	Spongostan Reembolized	Renal pelvic carcinoma Hematuria disappeared Doing well 3 months after first embolization
7	81	F	—	Bucrylate	Alive and in good shape 14 months after embolization
8	58	M	Multiple pulmonary Brain	Bucrylate	Angiography 8 months after embolization *renal artery still occluded* Pulmonary and possible brain metastases disappeared Alive and doing well 18 months after embolization
9	48	M	Multiple pulmonary	Spongostan + coils	Improved clinical condition Alive 3 months after embolization
10	59	M	Multiple skeletal	Spongostan + coils	Angiography 1 month after embolization renal artery occluded Improved clinically Alive 3 months after embolization

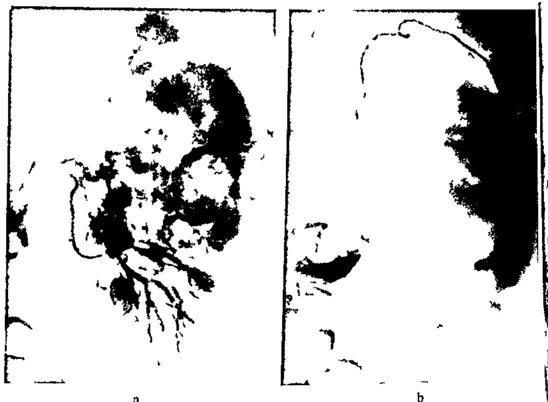


Fig 1 Case 8 a) Nephroangiography large hypervascular carcinoma in the left kidney b) 10 min after injection of Bucrylate the main renal artery is totally occluded A superior capsular artery remains open and probably contributes to the vascular supply of the tumour

ESR and anemia was found to have a large carcinoma in the upper pole of the left kidney with invasion of the left adrenal gland (Fig 2 a) and pulmonary metastases Superselective catheterization of the segmental arteries to the upper pole of the kidney was performed with subsequent embolization with Spongostan (Fig 2 b c) The tumour was partly fed from the left middle adrenal artery which was also catheterized and occluded Angiography 10 min after the embolization demonstrated marked reduction of the tumour circulation with preserved perfusion of the lower pole of the kidney (Fig 3 a) However repeat angiography one month later disclosed revascularization (Fig 3 b) and a new embolization was performed Another month later recanalization was again evident and at this occasion 2 metallic coils were placed in the renal artery in an attempt to obtain a permanent occlusion (Fig 3 c) The patient is clinically improved 3 months following the first embolization procedure His pulmonary metastases are unchanged

A 59 year old man (Case 10) was found to have a right renal carcinoma and multiple skeletal metastases In an attempt to palliate his local tumour symptoms (mainly pain) embolization was performed with Spongostan and two metallic coils were then placed in the main renal artery One month later the patient was clinically improved and feeling much better Angiography showed persistent occlusion of the



Fig 2 Case 9 a) Selective angiography of the left kidney large carcinoma in upper pole of the kidney At angiography of the left middle adrenal artery the adrenal gland was found to be invaded by tumour as well b c) Superselective angiography of segmental arteries to the upper pole of the kidney supplying the tumour These arteries were then embolized with Spongostan

right renal artery However the tumour was partly revascularized from lumbar arteries but the diameter of the tumour had decreased with 1 cm (Fig 4)

Two patients with renal pelvic carcinomas were embolized In a 67 year old female (Case 5) urography and angiography suggested renal pelvic carcinoma which was confirmed by fine needle aspiration biopsy Multiple pulmonary metastases were present and the patient was not considered for surgery Because of troublesome hematuria embolization was undertaken with Bucrylate (Fig 5) Hematuria dis appeared directly following embolization and angiography one month later showed



a



b



c

Fig 3 Same case as in Fig 2 a) Angiography 10 min after embolization arteries supplying the tumour are largely occluded Preserved perfusion of the lower pole of the kidney b) One month later The tumour is revascularized but the vascularity is somewhat reduced compared with Fig 2 a Reembolization with Spongostan was carried out but repeat angiography another month later again demonstrated revascularization c) 2 metallic coils are deposited in the renal artery which is almost totally occluded


a


b


c

Fig 4 Case 10 a) Nephroangiography vascular carcinoma medially in lower pole of the right kidney b) The renal artery is totally occluded with 2 coils c) One month later Late film from semiselective angiography Renal artery still occluded The accumulation of contrast medium within the tumour is caused by supply from lumbar arteries The diameter of the tumour has decreased with one cm

persistent occluded circulation to the kidney However the pulmonary metastases progressed and the patient died 3 months following embolization During these months she had no hematuria At autopsy the diagnosis of renal pelvic carcinoma was confirmed as well as multiple metastases in lungs liver and spine The embolized



Fig 5 Case 5 a) *Hypovascular* mass in upper pole of left kidney with encased artery (→) Percutaneous fine needle aspiration biopsy transitional cell carcinoma b) The renal artery is completely occluded with *Bucrylate*

renal artery was still occluded with deposits of Bucrylate and the kidney grossly infarcted Microscopy of the kidney disclosed residual vital infiltrating transitional carcinoma with invasion of blood as well as lymph vessels Another 66 year old woman (Case 6) with hematuria was found to have a renal pelvic carcinoma with multiple pulmonary metastases Hematuria stopped temporarily following embolization with Spongostan but recurred and at repeat angiography one month later revascularization had occurred Reembolization was performed and hematuria again disappeared This patient is free from urinary symptoms 3 months following embolization

Altogether 4 patients had macroscopic hematuria which disappeared after embolization In 2 (embolized with Spongostan and *Bucrylate respectively*) hematuria recurred however and reembolization was *performed again followed* by disappearance of hematuria

Four patients were embolized with *Spongostan and in 2 of these recanalization* was demonstrated at repeat angiography one month later One patient was nephrecto-

mized the same day because of severe pain This patient is alive 24 months later but pulmonary metastases have developed Six patients were embolized with Bucrylate. In one patient with a carcinoma in a horse shoe kidney causing severe hematuria partial recanalization had occurred at angiography one month later (the tumour had decreased in size) and further 6 months later the renal artery was again open At this time the patient had recurring hematuria and reembolization with Bucrylate was carried out Hematuria again stopped but the patient died 5 months later in progressive metastatic disease At autopsy the diagnosis was confirmed and the renal artery was found to be occluded Multiple metastases in lungs brain mediastinal and paraaortic lymph nodes were disclosed In 3 further patients repeat angiography 1 2, and 8 months after Bucrylate injection respectively demonstrated persistent occlusion of the renal artery

In 7 recent patients metallic coils were deposited in the renal artery following peripheral embolization with Spongostan in one persistent occlusion of the renal artery was found at angiography after one month

Four patients have died 10 days 3 8 and 12 months after embolization Three of these patients were at least temporarily relieved from local tumour symptoms

Complications

In one patient reflux of embolic material resulted in peripheral embolization of one k Embolectomy was performed but anuria developed postoperatively and the patient died 10 days after embolization This was the first patient in the series and no similar complication has later occurred However it is of major importance to be aware of this risk when injecting embolic material into the renal artery The second patient in the series developed severe pain over the embolized kidney why emergency nephrectomy had to be carried out This was a 55 year old female with known polycystic disease of the kidneys and a carcinoma in the left kidney The remaining 8 patients had moderate to severe local pain during 24 to 48 hours following the embolic occlusion This pain could be managed by analgesics sometimes including narcotics All patients also developed fever in some instances up to 39 5 C during the first days In most patients also nausea and vomiting occurred during the first 12 hours and a few developed a moderate paralytic ileus which however spontaneously disappeared after 48 hours In a few patients a transient mild hypertension developed in direct connection with occlusion of the renal artery but none of the patients had persistent blood pressure elevation

Discussion

When renal carcinoma is diagnosed 25 to 57 per cent of the patients already have metastases (SKINNER et coll 1971 LOKICH & HARRISON 1975) The natural course is unpredictable (EKELUND & JONSSON 1976) RICHES (1964) reported a series of 443

patients with renal carcinoma not considered for nephrectomy because of age and poor general condition, of whom 4.4 per cent were alive for 3 years and 1.7 per cent for 5 years. The median survival of patients with pulmonary metastases did not significantly improve following nephrectomy (JOHNSON et coll. 1975). The role of surgery is more evident when a solitary metastasis is present. In a recent series 50 per cent of the patients with a solitary metastasis resected before or after nephrectomy had a 5 year survival without adjuvant therapy (KLUGO et coll. 1977).

During recent years transcatheter embolization of the arterial supply of renal tumours has emerged as an alternative procedure for palliation of local tumour symptoms in patients not considered for surgery. ALMGÅRD et coll. reported on 19 patients with renal carcinoma treated with embolic occlusion using an autologous muscle suspension. The hematuria disappeared in 4 patients. All patients had a mild fever for the first 24 hours following the injection and several developed a moderate degree of pain and tenderness of the kidney during the first 2 days. Recently ALMGÅRD & SLEZAK reported on a series of 38 patients including the previous 19 (11 without subsequent nephrectomy). Five of the patients from the first report had died with survival periods ranging from 8 to 38 months after occlusion. Another large series consisting of 36 patients, 13 of whom were occluded before surgery, has been reported by GOLDSTEIN et coll. In all patients but one localized flank pain occurred lasting for an average of 48 hours. Parenteral narcotics were required for relief in many cases. Temperature elevations up to 39 C also occurred in virtually all patients for a similar duration. Moderate nausea, vomiting and paralytic ileus were also common. All these symptoms and signs which may be referred to as a "post embolization syndrome" were noticed to a varying degree also in the present 10 patients. GOLDSTEIN et coll. had 2 patients that developed renal failure following the occlusion, one resolving in 10 days but the other fatal. Microscopy of the non tumourous kidney in the latter case demonstrated evidence of tubular necrosis and the authors suggested that the large amount of contrast medium (approximately 300 ml) used during the combined diagnostic and therapeutic angiographic procedure was a contributing factor. As a result they recommended that the diagnostic angiography and the renal artery occlusion should be performed on separate days, which is now also the routine at this department. A second death in their series was caused by a large gas forming abscess developing within the infarcted tumour mass. In 12 of their 13 patients with arterial occlusion before nephrectomy the operation was considered facilitated. No follow up of the patients with arterial occlusion without subsequent operation was given. Several further reports substantiate the fact that preoperative occlusion of the tumour supply may facilitate nephrectomy (BEN MENACHEM et coll. 1975, BÜCHELER et coll., TURINI et coll. 1976, BERGREEN et coll., GIULIANI et coll.).

The other aspect of occlusion of the tumour supply is the ability to palliate local tumour symptoms, e.g. hematuria and pain. ALMGÅRD & SLEZAK thus reported immediate disappearance of severe hematuria in 10 patients and TURINI et coll. had

4 patients with hematuria disappearing 2 to 3 days after embolization The present series includes 4 patients in whom gross hematuria disappeared after the occlusion of the renal artery In altogether 8 of the 10 patients it appears justified to say that the quality of life especially regarding tumour symptoms was at least temporarily improved In one 58 year old man (Case 8) with presumably permanent occlusion of the renal artery (still occluded at angiography 8 months after Bucrylate injection) multiple pulmonary metastases and a possible brain metastasis have disappeared This patient is doing well 18 months after embolization However he has also been treated with progesterone and it is impossible to determine whether the improvement is due to embolization hormone therapy a combination of both or represents a spontaneous regression

Several embolic materials have been used for occlusion of the arterial supply of renal tumours autologous muscle suspension (ALMGÅRD et coll) gelfoam (GOLDSTEIN et coll BERGREEN et coll) Spongostan (TURINI et coll) isobuthyl 2-cyanoacrylate (GIULIANI et coll) and steel coils (WALLACE et coll 1976) Gelfoam and Spongostan (99 gelatin) are very similar and will only provide a temporary occlusion as well as autologous clot (BARTH et coll 1977) In 2 of the patients (Cases 6 9) total recanalization was found at repeat angiography one month after Spongostan occlusion Thus this and similar materials are not suited for permanent occlusion but excellent for short time preoperative obliteration A more permanent vascular occlusion is achieved by the use of isobuthyl 2-cyanoacrylate (Bucrylate) (DOTTER et coll 1975) GIULIANI et coll recently used this method for preoperative occlusion of the renal artery in 2 patients with renal carcinoma In the present series Bucrylate was employed in 6 patients In one patient partial recanalization of the renal artery was evident after one month why reembolization was carried out Six months later revascularization had again occurred and Bucrylate was injected once more At autopsy 5 months later the renal artery was found to be occluded In another 3 patients repeat angiography was performed 1 2 and 8 months respectively after Bucrylate injection showing persistent occlusion of the renal artery In this connection it is of interest to compare with the results of LUNDERQUIST et coll (1978) who used Bucrylate for obliteration of the gastric coronary vein and bleeding esophageal varices Percutaneous transhepatic portography in 8 patients 1 to 12 months later demonstrated recanalization of previously obliterated veins in 6 Thus Bucrylate does not cause a permanent vascular occlusion in all instances

WALLACE et coll developed a stainless steel coil with attached wool strands serving as a nidus for thrombosis to be deposited in the vessel to obtain permanent vascular occlusion This device is now manufactured in a complete set and was used together with Spongostan in 2 of the present cases In one patient at repeat angiography one month after the deposition of 2 coils in the renal artery it was still occluded However failure of the coil to cause permanent occlusion of the renal artery is on record (GIAVERI et coll 1978)

The effect of renal artery ligature on the growth rate of chemically induced

nephroblastomas in the rat was investigated by BISCHOFF et coll (1977) An immediate tumour cell death occurred secondary to ischemia and a marked reduction of tumour size and a decrease in tumour proliferation However, collaterals provided residual blood supply of tumour tissue and 70 days after the renal artery ligature still regions of obviously normal tumour cells were found Transcatheter arterial embolization should provide more peripheral occlusions and hence decrease the number of collaterals

It has been suggested that an immunologic response may be associated with the induction of tumour necrosis (ALMGÅRD et coll GOLDSTEIN et coll) However data are too few to be evaluated definitely at the present time and therefore a close follow up of patients subjected to renal artery embolization remains extremely important Whether or not the survival time can be improved, it is evident that local tumour symptoms may be palliated in patients with renal carcinoma who are not considered for surgery

Finally, it must be stated that transcatheter obliteration of the renal artery is combined with certain definite risks Reflux of embolic material with peripheral embolization may take place as in the first patient in the present series Displacement of the steel coil into the femoral artery has also been reported (HABIGHORST et coll 1977) The frequency of such complications is obviously reduced with increased technical experience and therefore a centralization of this kind of procedure is suggested

SUMMARY

Palliative occlusion of the arterial renal tumour supply was performed in 10 patients and the follow up is reported Nine of the patients had no subsequent nephrectomy Spongostan (99% gelatin) was used as the embolic material in 4 patients with the addition of steel coils in 2 Bucrylate was used in 6 cases Six patients are alive with survival rates presently ranging from 3 to 24 months after embolization Improvement of the survival time cannot be estimated but local symptoms such as hematuria and pain may be treated in those patients with renal tumours who are not considered for surgery

ZUSAMMENFASSUNG

Palliative Okklusion des arteriellen Zuflusses von renalen Tumoren wurde bei 10 Patienten durchführt und über deren Verlauf wird berichtet Neun der Patienten hatten keine nachfolgende Nephrektomie Spongostan (99 Gelatine) wurde als Embolusmaterial bei 4 Patienten verwendet unter Zufügung von Stahlringen bei zwei Bucrylat wurde in 6 Fällen verwendet Sechs Patienten leben mit gegenwärtigen Überlebensraten zwischen 3 und 24 Monaten nach der Embolisierung Eine Verbesserung der Überlebensrate kann nicht abgeschätzt werden jedoch können lokale Symptome wie Hämaturie und Schmerzen bei solchen Patienten mit renalen Tumoren behandelt werden die für eine chirurgische Behandlung als nicht geeignet befunden werden

RÉSUMÉ

L occlusion palliative des afférences artérielles de tumeurs rénales a été pratiquée chez 10 malades les auteurs présentent les résultats Neuf des malades n ont pas eu de néphrec

tomie ultérieure Du Spongostan (99 de gélatine) a été utilisé comme matériel d embolisa tion chez 4 malades avec addition de ressorts d acier chez 2 malades Du Bucrylate a été utilisé dans 6 cas Six malades sont en vie avec des durées de survie allant actuellement de 1 à 24 mois après l embolisation L amélioration de la durée de survie ne peut pas être estimée mais les symptomes locaux tels que l hématurie et la douleur peuvent être traités chez ces malades atteints de tumeur rénale inopérable

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ANGIOGRAPHIC FINDINGS IN ADRENAL MASSES

J HOEVELS and L EKELUND

The majority of malignant tumors metastasize to the adrenals (BURKE 1934) WILLIS (1934) observed adrenal blood borne metastases in 8 3 per cent of autopsies of 523 tumor patients BULLOCK & HIRST (1953) in a review of 19 700 post mortem examinations found tumor in 2 833 cases whereof 244 (8 6 %) had adrenal metastases ABRAMS et coll (1950) reported metastatic involvement of the adrenals in 27 per cent of 1 000 consecutively autopsied patients with carcinoma Certain types of tumors metastasize more readily to the adrenal glands In 175 autopsied cases of carcinoma of the breast and 160 cases of carcinoma of the lung adrenal metastases were found in 53 9 and 35 6 per cent respectively (ABRAMS et coll) Metastases to the adrenals from renal cell carcinoma are reported in 12 to 45 per cent at autopsy (ABRAMS et coll BENNINGTON et coll 1975 BULLOCK & HIRST GLOMSET 1938 KOZOLL & KIRSHBAUM 1940 SELBERG 1977 WILLIS 1948)

The incidence of adrenal metastases has received only marginal consideration in the angiographic literature (ALFIDI et coll 1969 KAHN 1967 KAHN et coll 1968 LANG 1973 REUTER 1968 ROSSI 1968 WRIGHT 1974 ZORNOZA et coll 1976) This may be due to the fact that most adrenal metastases are clinically asymptomatic or masked by the final stage of the primary disease and are detected first at autopsy Adrenocortical insufficiency because of metastatic infiltration of the adrenal glands is rare since the adrenal tissue is seldom completely destroyed (HAGTVET 1963) Further more there is no indication to look for adrenal metastases even if clinically possible when widespread tumor growth is present in other organs

Submitted for publication 12 December 1977

Table

Adrenal lesions in 34 patients

Adrenal metastases		11
Secondary growth from adjacent organs		3
Primary adrenal carcinoma		4
Pheochromocytoma		9
Bilateral adrenal pheochromocytoma	2	
Multiple unilateral adrenal pheochromocytoma	2	
Adrenal cortical adenoma		4
Bilateral adrenal cortical hyperplasia		2
Bilateral adrenal medullary hyperplasia		1
		34

As opposed to single reports on metastases abundant reports on primary benign and malignant adrenal tumors have appeared and their angiographic appearances have been described in detail. However, in most adrenal tumors reliable angiographic features do not exist for differentiation between a cortical and a medullary origin as well as between a benign and a malignant nature. Therefore the angiographic findings in secondary and various primary adrenal tumors were analysed and compared with the intention of finding out if a differential diagnosis of adrenal neoplasms by angiography is possible.

Material and Methods

The material comprised 31 primary and secondary adrenal tumors and 3 cases of bilateral adrenal hyperplasia in 34 patients, 22 women and 12 men ranging from 2 to 75 years of age (Table). All findings were confirmed either by operation or post mortem examination. Indications for angiography consisted of clinical evidence of hypertension or clinical and urographic suggestion of neoplasm, endocrinological evidence of adrenal disorder, and possible pheochromocytoma in patients with medullary carcinoma of the thyroid (SIPPLE 1961).

Adrenal metastases originated from ipsilateral renal carcinoma in 3 cases and from the contralateral kidney in 6 cases. In 2 patients with primary carcinoma of the ovary, the adrenal metastasis was found on the contralateral side. Adrenal cortical carcinoma and adrenal cortical adenoma were present in 4 cases each. Among the 9 patients with adrenal pheochromocytoma 2 cases had bilateral and 2 cases multiple ipsilateral pheochromocytomas. Two patients had bilateral cortical hyperplasia and one patient with medullary carcinoma of the thyroid and endocrinologically established pheochromocytoma had bilateral medullary hyperplasia as proven by microscopy (MONTALBANO et coll. 1962).

Abdominal aortography was performed in all but one of the 34 patients. In addi-



Fig 1

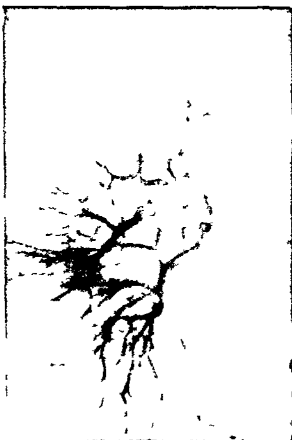


Fig 2

Fig 1 60-year-old female with hypovascular carcinoma of left kidney Selective angiography of right middle adrenal artery hypervascular metastasis to the adrenal gland with small amount of tissue preserved on top of lesion

Fig 2 Selective angiography of right kidney in 54-year-old male widened and tortuous pelvi ureteric arteries in renal pelvic carcinoma Hypovascular metastasis to adrenal gland

tion selective nephroangiography was performed in 21 cases The inferior and middle adrenal arteries were selectively catheterized in 6 and 16 cases respectively Adrenal phlebography was performed in all 3 cases of hyperplasia in 3 of the 4 cases of cortical adenomas and in 4 patients with pheochromocytoma The findings at adrenal phlebography are not discussed in this report All patients with a suggestion of pheochromocytoma had adrenergic blockade with phenoxybenzamine hydrochloride before angiography

Results

Metastases (11 cases) In 5 patients with renal carcinoma and one patient with carcinoma of the renal pelvis a metastasis to the adrenal gland was detected at the same occasion as the primary tumor In 3 additional patients with renal carcinoma and 2 patients with carcinoma of the ovary adrenal metastases were found 3 4 5 10 and 11 years respectively after detection of the primary tumor The size of the

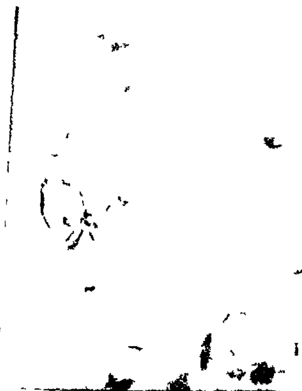


Fig 3 68 year old female with left nephrectomy 4 years previously because of renal carcinoma Selective angiography of right middle adrenal artery partly hypervascular metastasis in adrenal gland with prominent arterio venous shunting

metastases ranged between 2 cm × 2 cm and 12 cm × 8 cm Marked neovascularity was present in 7 of the 11 cases (Fig 1) whereas less newly formed vessels were demonstrated in 4 cases (Fig 2) Arteriovenous shunts were found in 5 cases (Fig 3) Accumulation of contrast medium in the capillary phase was marked in 2 tumors but moderate to faint in the majority of cases In most of the tumors hypovascular areas were present suggesting necrosis or cystic changes The middle adrenal artery being the main source of blood supply had an enlarged diameter of between 1 5 and 3 mm in 4 cases In 3 cases the only feeding vessel which could be identified was a moderately enlarged inferior adrenal artery An extraordinarily large metastasis (12 cm × 8 cm) was supplied by branches from 2 lumbar arteries in addition to a moderately enlarged middle adrenal artery

Secondary growth from adjacent organs (3 cases) A carcinoma in the upper pole of the kidney invaded the ipsilateral adrenal in 3 patients In one case (Fig 4) the enlarged middle adrenal artery was catheterized selectively Two renal carcinomas displayed multiple coarse vessels and arteriovenous shunting The same type of neovascularity was present within the affected adrenal gland In one case the renal carcinoma originated from the medial part of the upper pole of the kidney and invaded the adrenal gland which was replaced by a 13 cm × 14 cm mass The kidney itself was displaced caudally and its upper pole was tilted laterally Coarse tumor vessels were present within the renal carcinoma and in the lower part of the adrenal



a



b

Fig 4 48 year-old male with large carcinoma in upper pole of left kidney invading left adrenal gland a) Selective nephroangiography b) selective angiography of middle adrenal artery

mass whereas the middle and upper parts displayed fine but abundant neovascularity (Fig 5) In one patient with a huge right sided retroperitoneal sarcoma angiography suggested tumor growth within the inferior and lateral part of the ipsilateral adrenal (Fig 6) but at post mortem the right kidney and the right adrenal were found to be free of tumor growth

Adrenal cortical carcinoma Selective angiography was performed in 4 cases of adrenal cortical carcinoma The tumor size ranged from 5 cm × 5 cm to 10 cm × 13 cm Three of the patients were females 2 of whom presented with Cushing s syndrome The main feeding vessel had an enlarged diameter in all cases Marked neovascularity was present in 2 cases whereas a fine reticulated and sparse vascular network was found in the remaining 2 cases (Figs 7 8) Some arteriovenous shunting was de



Fig 5 Nephroangiography in 60 year old female kidney displaced caudally by huge partly hyper vascular mass Suggested radiologic diagnosis was primary adrenal tumor involving upper part of kidney but microscopy revealed primary renal carcinoma

monstrated in 3 of 4 tumors No evident accumulation of contrast medium durin the capillary phase was observed

Pheochromocytoma Among the 9 patients 5 had unilateral adrenal tumor Tw patients with Sipple s disease had bilateral manifestation of adrenal pheochromo cytoma In 2 cases multiple unilateral adrenal pheochromocytomas were presen Peripheral shell like calcification existed in one grossly degenerated pheochromo cytoma No malignant pheochromotycoma was encountered according to the stri criteria formulated by DAVIS et coll (1955) who stated that metastases should b present at the site where aberrant endocrine tissue is not otherwise found and th secretory function should be proven by the presence of the appropriate hormone i the metastases and their secretions Tumor size ranged between 1 cm × 1 cm an 20 cm × 15 cm with the majority of cases not exceeding 7 cm in diameter The degre of neovascularity was extremely different ranging from single tumor vessels in cases (Fig 9) and moderate neovascularity in 2 cases to marked hypervascularity i



Fig 6



Fig 7

Fig 6 58 year-old female with large retroperitoneal sarcoma Selective angiography of caudally displaced right kidney stretched capsular branches and abnormal vascularity corresponding to infero-lateral part of adrenal gland Autopsy extensive retroperitoneal sarcoma with no involvement of kidney or adrenal gland

Fig 7 2 year-old girl with Cushing s syndrome Selective angiography of left middle adrenal artery large partly hypervascular tumor with arterio-venous shunting Hypovascular area indicates necrosis Operation partly necrotic adrenal cortical carcinoma (Courtesy of Dr B Jacobsson Gothenburg Sweden)

3 cases (Fig 10) The tumor feeding adrenal arteries were enlarged in all cases Arteriovenous shunting was present in 3 tumors The appearance of the capillary phase varied greatly as far as intensity mode and duration of contrast accumulation are concerned In 3 cases the accumulation lasted more than 5 seconds whereas in the majority of cases the duration was less than 4 seconds

Adrenal hyperplasia (3 cases) Two patients with bilateral cortical hyperplasia presented with Cushing s syndrome Enlargement of the adrenal gland ranged between 3 cm × 6 cm and 6 cm × 10 cm Single abnormal arteries could be demonstrated in one hyperplastic adrenal gland within a circumscribed area (Fig 11) No arteriovenous shunting was evident and accumulation of contrast medium was inhomogeneous and of moderate intensity

Cortical adenoma (4 cases) The size varied between 2 cm × 1 cm and 5 cm × 5 cm Two patients presented with Cushing s syndrome One of the adrenal arteries the

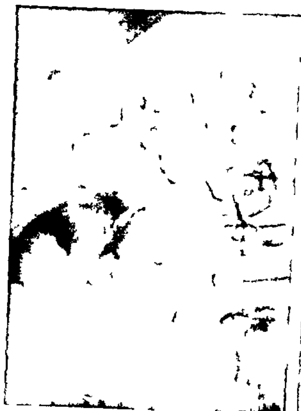


Fig 8



Fig 9

Fig 8 65 year old male with urographically suggested mass superior to right kidney Selective angiography of right kidney moderate number of abnormal vessels originating from somewhat widened inferior adrenal artery No arterio venous shunting Microscopy adrenal cortical carcinoma

Fig 9 59 year old male with large hypovascular pheochromocytoma with some arterio venous shunting in cranial part of tumor

main source of blood supply was enlarged in all cases Moderate neovascularity was present in 3 and hypervascularity restricted to the periphery in one of the tumors Arteriovenous shunting was found in one case (Fig 12) Accumulation of contrast medium during the capillary phase was extensive in 2 cases and slight in the remaining 2

Discussion

When performing adrenal angiography it should be borne in mind that the adrenal arterial system implies specific conditions which render most examinations to some degree incomplete In 4 extremely careful and comprehensive anatomic investigations an account is given of the adrenal blood supply (LEVI 1909 GERARD 1913 BUSCH 1954 MERKLIN & MICHELS 1958) Based on the results of cadaver examinations MERKLIN & MICHELS stated that the adrenal glands are not supplied by three single stem arteries but (1) 4 to 30 superior adrenal vessels of twig size derived from the inferior phrenic trunk or its posterior division (2) a middle adrenal vessel prevailingly



Fig 10 48 year-old female Selective angiography of middle adrenal artery hypervascular adrenal pheochromocytoma Small amount of preserved adrenal tissue evident cranially

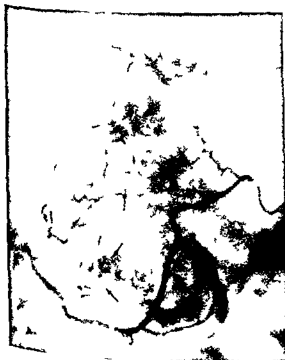


Fig 11 52 year-old male with Cushing s syndrome Selective angiography of left middle adrenal artery markedly enlarged adrenal gland with stretched arteries and small region with abnormal vascularity (→) Enlargement of the contralateral gland was demonstrated at same examination and adrenal hyperplasia was confirmed at microscopy following bilateral adrenalectomy



Fig 8



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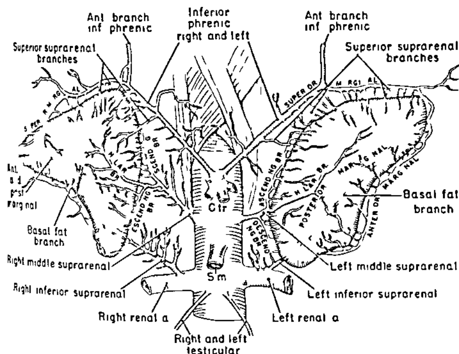


Fig 13 Composite drawing of the blood supply to the suprarenal gland (modified from Gérard 1913) General scheme of suprarenal arteries comprises inferior suprarenals which have slender collaterals terminals composed of anterior and posterior marginals and a basal fat branch middle suprarenal which has slender collaterals and ascending descending hilar posterior terminals superior suprarenals derived from phrenic trunk and its posterior division (Reprinted with the permission of the International College of Surgeons Chicago)

structures was demonstrated in 2 cases In addition to the varying degree of neovascularity the distribution of tumor vessels within the metastases demonstrated 2 different appearances Whereas in the majority of cases the vessels were evenly distributed throughout the metastasis they were mainly peripherally located in 2 cases Accumulation of contrast medium during the capillary phase was marked to moderate in 5 and slight in 6 cases

The adrenal tumor which has attracted most attention due to its clinical relevance is the pheochromocytoma In numerous publications a variety of angiographic features often quite contradictory have been described Abnormal vessels originating from the adrenal arteries displacement of adjacent arteries or organs accumulation of contrast medium within the tumor lesions (BOIJSEN et coll 1966 LANG et coll ALFIDI et coll COLAPINTO & STEED AGEE et coll 1973 MUHLHOFF et coll 1973 CHRISTENSON et coll 1976 LECKY et coll) hypertrophy of the suprarenal arteries combined with a fine network of small arteries with a reticular appearance (ROSSI et coll 1966 1968 ROSSI) are the angiographic abnormalities most often linked with adrenal pheochromocytoma The appearance of the capillary phase is described as



Fig 12 57 year old female with Cushing's syndrome Selective angiography of supplementary renal artery widened inferior adrenal artery supplying moderately vascularized adrenal mass with single arterio venous shunting Microscopy adrenal cortical adenoma

from the aorta but frequently lacking or replaced by another artery (3) an inferior adrenal vessel predominantly of single renal origin but in many instances multiple and of varied origin (aorta renal superior polar capsular branch of kidney) Variation of adrenal blood supply is the rule to such an extent that it is never the same in any two bodies or any two sides (Fig 13) Aortography and selective celiac nephro and adrenal angiography will usually provide information as to the main sources of blood supply degree of vascularity and size of the lesion (AHLBÄCK 1958 LANG et coll 1966 MUNSTER et coll 1966 PORSTMANN et coll 1966 KAHN & NICKROSZ 1967 ROSSI LANNER & ROSENCRANTZ 1970 COLAPINTO & STEED 1971 RESCHKE 1971 LECKY et coll 1976) In addition some conclusions as to demarcation or invasion of adjacent organs may be possible

Metastases to the adrenal glands may adopt the same degree of vascularity as the primary tumor (ALFIDI et coll ZORNOZA et coll) However in the present series 2 hypervascular renal carcinomas had hypovascular adrenal metastases On the other hand a hypervascular metastasis from a hypovascular renal carcinoma was seen in the contralateral adrenal Invasive growth from the adrenal metastasis into adjacent

et coll SHRAGO et coll 1974 SUTTON) describe a moderate to high degree of vascularity angiographic findings of avascular hypovascular adrenal cortical carcinomas are on record (COLAPINTO & STEED LECKY et coll FRITZSCHE et coll) The present 4 cases displayed varying degrees of neovascularity arteriovenous shunting being present in 3 The capillary phase was generally faint In 2 cases the angiographic findings correctly suggested invasive tumor growth into adjacent structures

Hyperplasia of the adrenal gland may be demonstrated at angiography (KYO RAK LEE et coll LECKY et coll) Microangiography (LAGERGREN) has revealed that the basic vascular appearance remains unchanged However parallel with the volume of the adrenal gland the size and number of vessels increase This is in keeping with the findings in the present 3 cases with bilateral adrenal hyperplasia However in one patient hyperplasia was diagnosed by angiography on only one side whereas the microscopy revealed hyperplasia of the contralateral adrenal gland as well No angiographic difference between cortical and medullary hyperplasia was found

Conclusion

Angiography of adrenal masses in general cannot provide any reliable information as to the nature of the lesion (MÜNSTER et coll 1966 RESCHKE 1971 KYO RAK LEE et coll LECKY et coll) Metastases cannot be distinguished from primary adrenal tumors In many instances it is not possible to differentiate by means of angiography between various benign and malignant adrenal tumors Angiographic features typical of adrenal pheochromocytoma do not seem to exist Adrenal hyperplasia may be present although angiography does not demonstrate enlargement of the gland However adrenal phlebography is the method of choice in these cases Invasion of the adrenal gland by malignancy in adjacent organs can render differentiation between adrenal and primary extraadrenal tumors impossible

SUMMARY

The angiographic findings in 34 patients with adrenal lesions were reviewed including 11 adrenal metastases 9 adrenal pheochromocytomas 4 adrenal cortical carcinomas 4 adrenal cortical adenomas 3 cases of adrenal hyperplasia and 3 cases of adrenal invasion from carcinoma of the upper pole of the kidney The results indicate differential diagnostic difficulties in distinguishing among these various entities by angiography

ZUSAMMENFASSUNG

Die angiographischen Befunde bei 34 Patienten mit Geschwulsten der Nebennieren (11 Metastasen 9 Phaochromozytome 4 kortikale Karzinome und 4 kortikale Adenome) und 3 Fallen von Hyperplasie werden analysiert und verglichen In 3 Fallen war ein Karzinom der Niere per continuitatem in die ipsilaterale Nebenniere eingewachsen Die differential diagnostischen Schwierigkeiten bei der Angiographie neoplastischer Prozesse werden hervorgehoben

homogeneous although at times irregular with a hypovascular zone (Rossi et col 1968) On the other hand some reports indicate considerable variation in vascularit (MUNSTER et coll FRY et coll 1967 LANNER & ROSENCRANTZ SUTTON 1975 BECKMANN et coll 1977) and a high incidence of hypovascular pheochromocytoma (ZELCH et coll 1974) Partial infarction of adrenal pheochromocytomas may occu and may be one reason for failure of demonstration of pheochromocytoma a angiography (BALTAXE et coll 1973) In 6 cases of pheochromocytoma examined by microangiography, hypervascularity was encountered in one case only (LAGERGREN 1967) The course of the feeding arteries around the periphery of the tumor was considered as typical in a series of 27 pheochromocytomas (LANNER & ROSENCRANTZ) In a series of 7 pheochromocytomas no correlation between the amount of vascularity and the presence or absence of malignancy was found (LAGERGREN) Taking into account all of these features the angiographic appearances of the present 9 cases of pheochromocytoma varied greatly making the identification of any reliable characteristics impossible Homogeneous accumulation of contrast medium of varying intensity was found in vascular tumors with enlarged feeding arteries encircling the mass as well as in cases with an even distribution of a fine reticular network of vessel within the tumor Large areas of necrosis appeared as hypovascular areas during the capillary phase in a few cases A shell like calcification partially encircling a mainly cystic pheochromocytoma was found in one case Four tumors were characterized by a low degree vascularity whereas 5 must be classified as hypervascular Arterio venous shunting was present in 3 cases

Carcinoma within the upper pole of the kidney with invasion of the ipsilatera adrenal gland rendered the adrenal indistinguishable from the primary tumor in cases Selective adrenal angiography demonstrated that adrenal tissue was destroyed and replaced by primary tumor tissue with its typical angiographic appearance I has recently been pointed out that the angiographic differentiation between adrena carcinoma and renal carcinoma is usually possible (FRITZSCHE et coll 1977) However differential diagnostic difficulties certainly may exist in distinguishing between these 2 entities as demonstrated in Fig 5

The angiographic features attributed to adrenal cortical adenoma range from hypervascularity to minimal neovascularity (LAGERGREN ALFIDI et coll KYO RA LEE et coll 1973 LECKY et coll) Considerable difficulties in differentiating cortical adenoma from adrenal pheochromocytoma have been pointed out (ROSSI) In a microangiographic investigation (LAGERGREN) the vascularity varied widely ranging from normal to entirely abnormal The angiographic findings in the present 4 case of adrenal cortical adenoma correspond well with the experience of other authors The degree of neovascularity was moderate in 3 cases and somewhat more developed in the fourth During the capillary phase the accumulation of contrast medium wa marked in 2 of the adenomas and slight in 2

Various opinions as to the angiographic appearance of adrenal cortical carcinoma are presented in the literature Whereas some authors (KAHN & NICKROSZ ALFID

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RÉSUMÉ

Les auteurs ont passé en revue les signes angiographiques chez 34 malades atteints d lésion surrénalienne comprenant 11 métastases surrénaliennes 9 phéochromocytomes surrénaliens 4 carcinomes de la cortico surrénale 4 adénomes cortico surrénaliens 3 c d hyperplasie surrénalienne et 3 cas d envahissement de la surrénale par un carcinome d pole supérieur du rein Les résultats de cette étude montrent les difficultés du diagnosti différentiel angiographique entre ces différentes affections

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ANGIOGRAPHY OF THE TESTICULAR ARTERY

IV Magnification angiography in intrascrotal abnormalities

L NORDMARK and G NYBERG

Clinical examination of the testis and epididymis might seem a simple matter in view of the position of these organs in the scrotum However experience has shown that it is often hard not to say impossible to secure an accurate diagnosis solely by palpation and trans illumination with a lamp (SCORER & FARRINGTON 1971 FROHMÜLLER 1973 MUKERJEE et coll 1975 RILEY et coll 1976 WILLIAMSON 1976) In order to gain an idea of the diagnostic value of angiography of the testis this examination was carried out in cases with different pathologic conditions in the scrotum Magnification angiography was used in order to facilitate the evaluation of small vessels. No previous reports have been published on magnification angiography in patients with abnormalities in or in the vicinity of the testis

Previous examination methods

Both the testis and the epididymis are readily accessible for palpation and expanding lesions can be examined by trans illumination with a lamp to determine whether they are filled with fluid In uncertain cases the testis must be explored unless some other form of examination gives the correct diagnosis Fine needle biopsy may be performed but this involves the risk of tumor spreading or hemorrhage and also that the biopsy material may not be representative

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Table 1

Final diagnosis in the 42 testicles examined (in some cases several diagnoses were made at the same time)

Final diagnosis	Number
Hydrocele	12
Spermatocele	4
Hematoma	5
Epididymitis	12
Torsion	4
Seminoma	3
Embryonal carcinoma	1
Benign adenomatoid tumor	1
Varicocele	1
Testicular atrophy	3
Partial necrosis of the testis	1
Tight fibrosis around the testicle	1
Normal	2

In 14 testicles angiography could not be performed adequately In one case this as due to subintimal injection of the contrast medium into the testicular artery and n another to slight extravasation of the medium due to a vascular rupture some entimeters from the catheter tip in 4 cases the testicular artery originated from the enal artery and could not be examined selectively In 8 cases it was not possible to atheterize the testicular artery 2 of these patients were aged 20 and 43 while the thers were over 57

The examinations were considered excellent if the centripetal arteries were visible the entire testis or at least in its relevant part It was considered satisfactory if the ratesticular arteries were sufficiently well demonstrated to allow an approximate aluation and poor if no assessment of these arteries was possible Low magnifica on, imperfect free projection from superimposed structures and an unsuitable posi on of the testicle rendered the evaluation of the films difficult In patients with rge hydroceles or other large expanding lesions the position of the testicle could ot be influenced by adjustments

Results

In the 42 testicular angiographies performed the result was considered excellent 31 satisfactory in 9 and poor in 2 instances In the latter 2 examinations one ferred to a patient with a high placed testicle which could not be exposed free from perimposed structures and the other to a patient with a large scrotal hematoma hich was compressing the vessels in the funiculus so that the flow rate was extremely ow

In the assessment of the films the differences were noted between the angio- raphies from the pathologic cases and the normal angiographic appearances as

Thermography of the scrotum gives information on differences in blood flow between the two halves of the scrotum (KORMANO et coll 1970 RUDOLPH et coll 1972 SELVAGGI et coll 1973 LEE & GOLD 1976)

Flow measurement using ultrasound and the Doppler technique is another way of evaluating the circulation The method has been used for differentiating between epididymitis and testicular torsion (MILLFRET & LIARAS 1974 LEVY 1975, PEDERSEN et coll 1975 THOMPSON et coll 1975 PERRI et coll 1976)

Scintigraphy of the scrotum has been performed on various indications demonstrating the activity within the entire scrotum or parts of it (DATTA & MISHKIN 1975 HAHN et coll 1975 MUKERJEE et coll, HITCH et coll 1976 RILEY et coll)

Soft tissue radiography of the scrotum and its contents has been described by a few authors Calcifications (JUILLARD & KERMAREC 1969 JUILLARD et coll 1972) as well as expanding lesions (PRICE & LOVEDAY 1975) have been demonstrated

Phlebography of the testicular vein with injection of the contrast medium into the left renal vein and the patient in the standing position was performed by AHLBERG et coll (1966) in patients with varicocele The entire testicular vein as well as the varicocele filled in these patients whereas in a control group of healthy subjects the entire testicular vein was not filled COMHAIRE & KUNNEN (1976) injected the contrast medium instead selectively into the left testicular vein through a catheter inserted from the right groin

GÖSFAY (1959) and BROWN et coll (1967) also reported having performed phlebography in the testicular vein in patients with varicocele but they injected the contrast medium in connection with surgery directly into the testicular vein immediately above the internal inguinal ring

BRODNY et coll (1955) demonstrated that angiography of the testicular artery could be carried out in connection with surgery The artery was punctured after exposure at the base of the scrotum A single view was obtained immediately after the contrast medium had been injected No practical application for this method could be found by these authors

Material and Methods

An attempt at angiography was made in 51 patients aged between 13 and 71 years 46 unilaterally and 5 bilaterally i e 56 testicles were to be examined The indication for angiography was an inconclusive finding at palpation or a possible testicular tumor

In all cases the aim was to perform magnification angiography of the testis on the relevant side Local anesthesia was used in all except the youngest patient who was examined under general anesthesia Three ml metrizamide 350 mg I/ml (Amipaque Nyegaard) were injected manually into the testicular artery through a catheter inserted via the right femoral artery The degree of magnification was between 2 and 3 times The technique has been described in detail by NORDMARK (1977)

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In the assessment of the films the differences were noted between the angiographies from the pathologic cases and the normal angiographic appearances as



Fig 1 Hydrocele in a 32 year old man Subtracted magnification Mass on the left side in the scrotum It could be trans illuminated and measured 10 cm × 15 cm The left testicle could not be palpated Angiography Normal testicle (→) surrounded by a hydrocele (↠) Artery in the tunica vaginalis (⇻)

Fig 2 Hydrocele increasing in size over several years in a 54 year old man Subtracted magnification Angiography Hydrocele Artery in the tunica vaginalis (↠)

described by KORMANO & NORDMARK (1977) The final diagnosis was often based on the operative findings and also in 60 per cent of the cases on microscopy of biopsy material obtained at exploration or of the entire testis and epididymis In 9 cases it was possible in the light of the angiographic finding to postpone the operation The clinical course later confirmed the angiographic diagnosis The final diagnosis in these cases was hematoma in 5 and epididymitis in 4 instances (Table 1)

Hydrocele In hydrocele the collection of fluid lies between the two layers of the tunica vaginalis The vessels of the parietal layer become displaced from the testis when fluid is accumulated between the two layers The arteries in the tunica vaginalis consist of vessels running from the tunica vaginalis branch which originates from the testicular artery a few centimeters cranial to the testis and which usually is well demonstrated even if no hydrocele is present (KORMANO & NORDMARK) It has communicated through a wide anastomosis with one of the arterial branches on the sur



Fig 3 Hematoma in the funiculus in a 21 year-old man Blow to the left groin 10 days earlier Subtracted magnification Angiography a) Arterial phase Rapid accumulation of contrast medium in the funiculus (→) The epididymis is widened with contrast filled arteries (↔) b) Venous phase Numerous wide veins in the funiculus and epididymis Testis appears to be normal (→)

face of the testis at the lower testicular pole Using magnification angiography it has not been possible to demonstrate any other form of blood supply to the tunica vaginalis (Figs 1 2) The vessels of the tunica membrane were displaced but no other changes were observed either in the tunica vaginalis or in the testis and epididymis in patients with pure hydrocele

Spermatocele In 4 patients a spermatocele was found at operation The largest had a diameter of approximately 1 5 cm and the others were very small In no case could any abnormalities connected with a spermatocele be demonstrated at angiography

Hematoma was present in 5 patients One had a hematoma of the funiculus due to trauma Angiography revealed a widened funiculus which rapidly showed a diffuse accumulation of contrast medium (Fig 3 a) The epididymis also was widened and a number of arteries filled within the entire epididymis A large number of veins in both the funiculus and the epididymis also filled with contrast medium (Fig 3 b)

Two patients had a traumatic hematoma around the testicle which had originated 4 and 7 weeks earlier respectively and one had a liquified hematoma following an

Table 2

The 11 patients with epididymitis arranged after time between onset of symptoms and angiography. Films were exposed 2, 4, 6, 9, 13, 19, 25 and 28 seconds after start of injection

Weeks after onset	Width of testicular artery (mm)		Seconds after start of injection			
	Affected side	Healthy side	Contrast medium reached testis	Start of accumulation in epididymis	Veins in the epididymis appeared	Veins in testis appeared
1	1.1	0.9	2	4	9	25
1	2.0	1.2	4	6	9	19
1	1.4	1.4	2	4	9	13
2	1.6	1.4	4	9	13	25
2.5	2.2	—	4	9	13	>13*
2.5	1.8	1.6	4	9	19	25
3	1.5	1.4	2	9	13	25
3	1.3	1.3	2	6	9	19
4	1.5	—	4	6	9	19*
8	1.8	1.1	4	6	13	19
8	0.9	1.1	4	6	13	25
13	1.5	1.5	2	9	19	19

* The last views in the series were not assessable due to a technical mishap.

operation for hydrocele 6 months earlier. In these cases the hematomas were situated between the tunica vaginalis and the wall of the scrotum. No vessels from the testicular artery were displaced. Only an increased distance between the testicle and the scrotal wall was apparent at angiography (Fig. 4).

In one patient with a hematoma the size of a clenched fist following an operation for hernia 7 weeks earlier, the condition had been interpreted clinically as a recurrence of the hernia. At angiography, the circulation was found to be so slow that the testis could not be assessed. Even after 30 seconds, no artery in the testicle or the epididymis had filled.

Epididymitis. Eleven patients had epididymitis. In one of them it was bilateral, developing first on one side and 1.5 weeks later on the other side. In Table 2, the cases have been divided up according to the time that had elapsed after the onset of the inflammation. The width of the testicular artery is also given, as well as the interval elapsing between the start of the contrast injection and the times when the medium reached the testis, when contrast accumulation began to appear in the epididymis and when veins in the epididymis and testis began to fill.

Normally, no contrast is to be seen in the body and tail of the epididymis (KORMANO & NORDMARK). In patients with epididymitis, the arteries and the parenchyma



Fig 4



Fig 5

Fig 4 Scrotal hematoma in a 2? year-old man One month earlier trauma to the scrotum Subtracted magnification Angiography Increased distance between testis (→) and scrotal wall (↔) No vascular displacement A few contrast filled veins around the lower pole of the testis At operation a hematoma around the testis and cicatricial tissue around the lower testicular pole were found

Fig 5 Receding epididymitis in a 26-year-old man Subtracted magnification Rapid filling of veins in the entire epididymis which is widened (→)

Fig 6 Residues after epididymitis 8 weeks earlier in a 39 year old man Now subjective feeling of a mass on the left in the scrotum Hard painless mass measuring 1 5 cm × 1 5 cm palpated in the lower testicular pole Angiography Tail of epididymis (→) widened The veins filled rapidly At operation, the tail was thick and hard Microscopy of the tail revealed chronic epididymitis



the entire epididymis filled rapidly with contrast medium it was also widened nd its veins filled sooner than those in the testis (Fig 5) The veins in the epididymis d not fill more rapidly in patients with acute epididymitis than in those with receding flammation On the other hand the degree of the accumulation of the contrast edium as well as the number and width of the veins that filled depended on the ration and intensity of the epididymitis prevailing at the time of examination e thicker the epididymis and the greater the number of filled veins the more easily uld the epididymis be distinguished from the testis

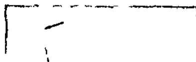


Fig 7

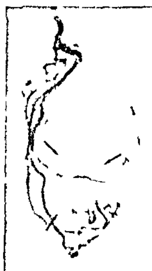


Fig 8 a

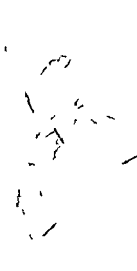


Fig 8 b



Fig 9

Fig 7 Torsion in a 19 year old man with swelling of the right testicle for 1 5 months erroneously considered as epididymitis Angiography No contrast medium passed down to the testicle Small vessels filled in the funiculus around the right testicular artery (→) At operation necrosis of the testis and epididymis were found as a result of the torsion

Fig 8 Seminoma in a 41 year old man who for 2 months had noticed that the lower half of his left testicle had become slightly larger and harder Subtracted magnification a) Angiography The normal centripetal arteries are well demonstrated in the upper half of the testis but not in the lower pole In the latter area only a few irregular vessels (→) b) Angiography of specimen Seminoma (→)

Fig 9 Seminoma in a 52 year old man with uncertain findings at palpation after a recent epididymitis Subtracted magnification Angiography No normal intratesticular arteries Microscopy Entire testicle was composed of a seminoma

In patients in whom the inflammation had disappeared except in one small area the veins in that particular area filled more completely and thus abnormally well than in the other parts of the epididymis (Fig 6)

In the patients with acute epididymitis the artery on the affected side was wider than on the other side The width of the testicular artery was the same on both sides in patients with receding inflammation

Torsion was present in 4 patients The condition had clinically been erroneously diagnosed as epididymitis The symptoms had begun in one patient 5 days earlier and in the 3 others 7 to 10 weeks earlier The testicular artery filled down to the level

of the twist d area and gradually the contrast medium passed into small vessels in the funiculus None of the medium passed into the vess-ls in and around the testis (Fi. 7) Microscopy reveal-d necrosis of the testis and epididymis due to arterial torsion No difference in the diameter of the testicular artery between the affected and the healthy side was noted in these cases

Testicular tumor Tumors of the testis consist in 90 per cent of cases of malignant germ-cell tumors (FROHMULLER) and with respect to the microangiographic aspect two groups may be distinguished (ICHIJO 1975) One group consists of pure semi nomas which are poorly vascularized and the other of teratomas and carcinomas of various types most of them highly vascularized Mixed tumors usually belong to the latter group

In the present material there were 3 pure seminomas These tumors contained no normal vess ls and were less vascularized than the surrounding testicular tissue The vessels in th tumor were narrow with pathways differing compl-tely from the regular course s en in testicular tissu- (Figs 8 9) The accumulation of contrast medium within the tumor seemed not to differ from that in normal testicular tissue Th testicular artery was not wider on the affected side

As regards the highly vascularized tumors the pres-nt material contained only one embryonal carcinoma The tumor measured 10 cm × 8 cm 7 cm and h.d grown very rapidly The entire testis and epididymis was infiltrated by the tumor and necrotic areas were present in the centre At angiography a fairly large numb r of irregular vessels filled within the tumor but few vessels were seen in the centre of the tumor (Fig 10 a) The width of the vessels varied and the accumulation of contrast m dium was irregular but on the whole was more intense than in seminomas and normal testes (Fig 10 b) Normal testicular vessels were not visible The epididymis could not be identifi d The testicular artery was wider than normal measuring 3 mm in width on the tumor side while on the other side its width was normal (Fig 10 c)

One patient had a bean sized benign adenomatoid tumor in the tunica albuginea No angiographic abnormalities were observed although the films were of excellent qu lty

Varicocel One patient with varicocele was examined The testis was smaller than normal and above all narrower (Fig 11 a) The testicular artery was of ordinary width Six seconds after the contrast medium had reached the testis the wide veins in th varicocele began to fill This time is as short as that elapsing when epididymal veins fill in epididymitis and 2 to 3 times as rapid as for normal testicular veins (Table 2) The veins in the varicocele were roughly twice as wide as the main trunk of the testicular artery (Fig 11 b) The varicocele was in this patient composed of both the pampiniform and the cremasteric plexus mainly the latter The efferent veins in the funiculus began to fill about 20 seconds after the contrast medium had reached the testis but a large amount of medium was still present in the wide veins in the varicocele after 70 seconds



Fig 7

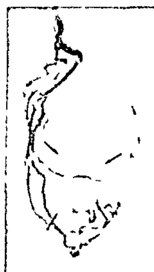


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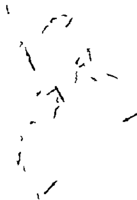


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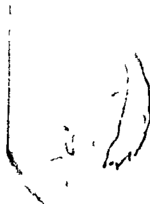


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In patients in whom the inflammation had disappeared except in one small area the veins in that particular area filled more completely and thus abnormally well than in the other parts of the epididymis (Fig 6)

In the patients with acute epididymitis the artery on the affected side was wider than on the other side The width of the testicular artery was the same on both sides in patients with receding inflammation

Torsion was present in 4 patients The condition had clinically been erroneously diagnosed as epididymitis The symptoms had begun in one patient 5 days earlier and in the 3 others 7 to 10 weeks earlier The testicular artery filled down to the level



Fig 11 Varicocele in a 35 year-old man for one year with a feeling of heaviness in the left half of the scrotum Subtracted magnification Angiography A narrow testicle (→) and early filling of wide veins caudal to the testis Later wide veins in the funiculus also filled a) Arterial phase b) Venous phase Pampiniform plexus (+→) Cremasteric plexus (++→)

Other conditions In one patient half the testis was necrotic following a recent epididymitis and orchitis No blood vessels filled in the necrotic area (Fig 12) In the lower pole the intratesticular vessels were normal

One patient had developed ring shaped cicatricial fibrosis around the middle of the testis following an earlier operation for hydrocele This caused a slow circulation in the lower half of the testis which felt much harder on palpation than the upper half (Fig 13) No other angiographic abnormalities were established

Discussion

Different methods have been tried for improving the possibilities for diagnosis of diseases and lesions of the scrotal contents without recourse to operation Thermography will demonstrate increased or decreased circulation in the organs within the scrotum This method however would seem to be fairly approximate and unspecific and it cannot provide information regarding the reason for the change in blood flow nor does it allow a differentiation between an intra and an extratesticular lesion An evaluation will be difficult furthermore if the circulation in the other half of the scrotum is not normal

Ultrasonic examination of the blood flow to the testis should be the simplest method for diagnosing acute torsion However a reactive hyperemia seems to

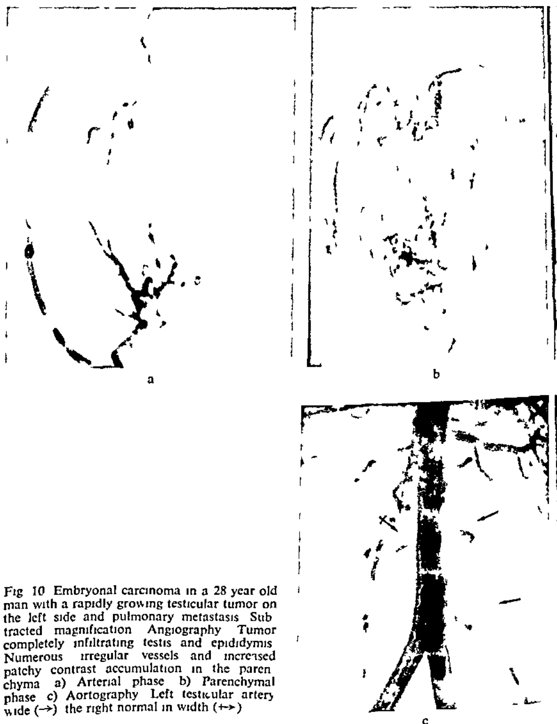


Fig 10 Embryonal carcinoma in a 28 year old man with a rapidly growing testicular tumor on the left side and pulmonary metastasis Subtracted magnification Angiography Tumor completely infiltrating testis and epididymis Numerous irregular vessels and increased patchy contrast accumulation in the parenchyma a) Arterial phase b) Parenchymal phase c) Aortography Left testicular artery wide (→) the right normal in width (↔)

Atrophy was present to a moderate degree in 3 testes (Fig 11 a) These were smaller and softer than normal but no abnormalities were evident at angiography except that the testes were relatively small No abnormality of the intratesticular vessels could be observed

normalities Several conditions are not included in the material which also is rather small However the observations have been typical in most of the lesions examined and thus motivated a report

Hydrocele was readily demonstrated except in cases with very small collections of fluid—less than 10 ml If the only finding was an increased distance between the testis and the scrotal wall it was not possible to differentiate the condition from a hematoma in the scrotum In addition to the demonstration of hydrocele the testis and epididymis could also be assessed It should thus be possible to diagnose a testicular tumor in patients with hydrocele When the hydrocele was large assessment was sometimes difficult if the position of the testis was unfavourable and could not be altered In such cases the epididymis and testis were sometimes superimposed which limited the possibility of diagnosing the conditions within the testicle

Small spermatoceles could not be demonstrated As the wall of a spermatocele does not contain large vessels the large spermatoceles will presumably not give characteristic angiographic abnormalities either

Hematomas in the scrotum usually arise after a trauma When the hematoma is situated between the tunica vaginalis and the wall of the scrotum abnormalities other than an increased distance between the testis and the scrotal wall are not to be expected On the other hand if the blood is situated between the layers of the tunica vaginalis the appearances will be the same as in hydrocele Large hematomas may cause pressure on the vessels and slowing of the circulation Hematoma in the funiculus may give rise to widening of this structure with venous stasis (Fig 3 b)

Epididymitis produced evident angiographic abnormalities The more acute the inflammation the greater was the accumulation of contrast medium in the epididymis the wider it was and the greater was the number of wide veins filled with medium in the whole or parts of the epididymis In acute epididymitis the testicular artery was wider on the affected side Most of the patients with epididymitis were referred for examination because of an uncertain localization of a palpable mass or the possibility of a malignant tumor when the inflammation did not subside in the usual way within the entire epididymis (Fig 6) In these cases angiography usually gave clear information that the palpable mass was situated in the epididymis and not in the testis and that the testis was normal Exploration was therefore not performed

Circulatory impairment in the testis can be demonstrated by angiography This condition may be due to a reduced flow in the testicular artery resulting from operation for hernia orchidopexy tumor or a hematoma Impaired circulation is an indication for surgical exploration

Torsion of the testis can be diagnosed with angiography Other causes of arrested circulation than torsion have been described but apparently are rare (WILLIAMSON) The risk of mistakes in the differential diagnosis would thus seem to be slight but whatever the diagnosis indication for operation remains

Seminomas are poorly vascularized If these tumors are to be demonstrated at angiography the films must be of such good quality that the intratesticular vessels



Fig 12 Partial necrosis of the testis in a 24 year old man with swelling and tenderness on the left side of the scrotum for one week Subtracted magnification Clinical suggestion over looked torsion but flow measurements with ultrasound demonstrated normal flow Angio graphy Half the testis without circulation (→) Normal intratesticular vessels in the lower pole Epididymis widened with increased blood flow as in epididymitis

Fig 13 21 year old man previously operated upon twice for hydrocele Subtracted magni fication The upper half of the testis was normal on palpation the lower half harder than normal Angiography Normal appearances in upper half of testis slow circulation in lower half At operation constrictive fibrosis around the middle of the testis between the two halves and venous stasis caudal to the fibrosis Normal conditions were reinstated after removal of the fibrosis

develop around a necrosed testis some time after the torsion (PEDERSEN et coll PERRI et coll) and the condition may then be erroneously considered as epididymitis

Scintigraphy also gives information about the circulation but this method as well gives only a relatively rough approximation and is unspecific However it gives definite information as to whether torsion or epididymitis are present a result which in many cases has been found hard to achieve clinically (HAHN et coll MUKERJEE et coll HITCH et coll RILEY et coll) An abscess in the testis or epididymis can also be demonstrated (DATTA & MISHKIN RILEY et coll)

Microcalcifications in seminomas may be demonstrated with soft tissue radio graphy (JUILLARD & KERMAREC JUILLARD et coll) Their films had been exposed with 30 kV In the present material microcalcifications were not demonstrated in the seminomas but might have been present but not visible on the films as 70 kV was used for the angiographies It does not seem likely that soft tissue radiography as a rule can give more information than what is obtained with palpation and trans illumination with a lamp However if calcifications are demonstrated these may sometimes explain unclear findings from palpation

In varicocele phlebography of the testicular vein is superior to all other methods for obtaining full information on the venous anatomy before an operation (COM HAIRE & KUNNEN) Its value for other scrotal abnormalities has not been documented

The present report describes the angiographic findings in different scrotal ab

RESUME

L'angiographie agrandie du testicule avec injection selective dans l artere testiculaire a . pratiquee chez des malades ayant differentes lesions du scrotum soit reelles soit supposees. On a trouvé des aspects angiographiques caractéristiques dans l epididymite la torsion du testicule les tumeurs les hematomes et l hydrocele

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can be assessed at least within the part of the testis believed to be involved For this it is necessary in some cases for the position of the testis to be altered without affecting the circulation The spontaneous position of the testis sometimes for instance, gives rise to an axial projection and there is then no possibility of distinguishing a small seminoma

Small, highly vascularized testicular tumors are probably diagnosed more easily at angiography but as such tumors are not included in the present material it is too early to make an evaluation on this point On the other hand the present results indicate that with preoperative testicular angiography it is possible to differentiate between a seminoma and an embryonal carcinoma

Varicocele has such a characteristic angiographic appearance that it is readily diagnosed correctly (Fig 11) The contrast medium remains for a long time in the varicosed veins AHLBERG et coll stated that in their series contrast medium was always still present in these veins 100 seconds after injection of the medium into the left renal vein with the patient in the standing position In the present series it was found that the circulation through the varicocele is also slow in the recumbent position

The case in the present series with constrictive fibrosis around the testis after an operation (Fig 13) indicates that postoperative palpatory findings that are difficult to evaluate may be explained with the aid of magnification angiography In this patient normal configuration and consistency were reinstated after surgical treatment of the fibrosis

Thus it would seem that magnification angiography of the testicular artery in vivo makes it possible to diagnose accurately a number of different abnormal conditions in and around the testis Interest was concentrated on establishing the angiographic appearances in the different conditions The findings indicate that magnification angiography might be a valuable complementary method in the investigation of scrotal and funicular lesions

SUMMARY

Magnification angiography of the testis with selective injection into the testicular artery has been performed in patients with different lesions in the scrotum either real or suggested Characteristic angiographic appearances were found in epididymitis testicular torsion tumor hematoma and hydrocele

ZUSAMMENFASSUNG

Die Vergrosserungsangiographie des Testis mit selektiver Injektion in die Testikelarterie wurde bei Patienten mit verschiedenen vorhandenen oder vermuteten Lasionen des Skrotums durchgefuhrt Charakteristische angiographische Bilder bei der Epididymitis einer Testikeltorsion bei Tumoren Hamatomen und Hydrocele wurden gefunden

RÉSUME

Langiographie agrandie du testicule avec injection sélective dans l artère testiculaire a ete pratiquee chez des malades ayant différentes lésions du scrotum soit réelles soit supposees. On a trouve des aspects angiographiques caracteristiques dans l épididymite la torsion du testicule les tumeurs les hematomes et l hydrocèle

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SOMATOSTATIN IN COMPUTER TOMOGRAPHY OF THE ABDOMEN

S EFENDIC O MATTSSON and R LUFT

In computer tomography with an exposure time that may amount to several seconds, it is of great advantage that the organs move as little as possible This is particularly of value at computer tomography of the abdomen as otherwise artefacts appear due to intestinal movements (GOODENOUGH et coll 1975 BELZER & HUANG 1977 KOWALSKI & WAGNER 1977 WAGNER 1977) As somatostatin is known to inhibit gastric emptying (BLOOM et coll 1975 JOHANSSON et coll 1978) as well as intestinal motility (EFENDIĆ & MATTSSON 1978 JOHANSSON et coll) an attempt was made to administer this drug to improve the quality of the CT scans of the abdomen

Computer tomography of the abdomen was performed in 6 patients first without somatostatin and immediately thereafter the peptide was administered and repeat scans obtained The apparatus used was a Delta Scan 50 (Ohio Nuclear) with a relatively long exposure time (about 2 min) Somatostatin 200 μg was given to the patients who had fasted overnight as a bolus followed by continuous intravenous infusion of 7 μg min during 15 to 30 min

In general the quality of the scans was improved in the sections made during infusion of somatostatin As evident from Figs 1 and 2 the artefacts the disturbing streaking phenomena were considerably reduced after administration of somatostatin Furthermore the appearance of the abdominal cavity in consecutive sections was more stable when the peptide was given This resulted in better delineation of the abdominal

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Based on a report given at the XIV International Congress of Radiology Rio de Janeiro 1977
Submitted for publication 16 May 1978



Fig 1 Case with suggested aldosterone producing adrenal tumor a) Normal motility Artefacts produced by intestinal movement b) After somatostatin infusion



Fig 2 a) Normal motility b) After somatostatin infusion

organs The same results were achieved in the other 4 patients No side effects occurred in the present series

Somatostatin is a tetradecapeptide widely distributed in the body in endocrine like cells, such as in the pancreas thyroid and gastrointestinal tract as well as in nervous tissue (HÖKFELT et coll 1975) Wherever present—at least in endocrine or endocrine like cells—it exerts inhibitory action Thus its inhibitory effects on the release of gastrointestinal hormones were early recognized (EFENDIĆ et coll 1978) Recently the inhibitory effect on the motility of the gastrointestinal tract was reported (EFENDIĆ & MATTSSON) At computer tomography of the abdominal organs the motility of the gastrointestinal tract especially the air containing parts is a disadvantage In comparison with other agents known to inhibit gastrointestinal motility

somatostatin has the advantage to be well tolerated and to have an easily regulated action Thus the motility of the gut was almost completely arrested 5 min after beginning of the infusion and re established 5 min after its discontinuance (EFENDIĆ & MATTSSON) Therefore somatostatin may be the drug of choice for improvement of the quality of abdominal CT scans Further experience is however needed for estimation of the most suited dosage

SUMMARY

Intravenous infusion of somatostatin as an aid in reducing artefacts in computer tomography caused by intestinal movement is described

ZUSAMMENFASSUNG

Intravenose Infusion von Somatostatin als Hilfsmittel zur Reduzierung von Artefakten bei der Computertomographie die durch Darmbewegungen verursacht sind wird beschrieben

RESUME

Les auteurs decrivent la perfusion intraveineuse de somatostatine pour réduire les artefacts causes par le mouvement intestinal en tomographie assistee par ordinateur

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Fig. 2. a) Normal motility. b) After somatostatin infusion.

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Table

Age and sex distribution

Age (years)	Females	Males
30–40		1
40 50	4	3
0–60	4	7
60–70	7	15
70–80	16	18
80–90	12	8
90–100	1	

recognized metabolic bone disease hyperparathyroidism or osteomalacia The age and sex distribution is given in the Table

After removal of the viscera a frontal slice 1 cm thick of the body of the second and third lumbar vertebra was chiseled out The bone marrow parenchyma and fatty tissue were washed out by hot water and the remaining framework of bone tissue was stored in formol 4 % Due to tearing of the specimen it was not possible to properly evaluate 8 of the 97 cases The remaining 89 cases were evaluated subjectively According to the amount of trabecular bone tissue present each specimen was graded from 1 to 6 highest score indicating highest bone mass (Fig 1) Scores 4 and higher indicate normal bone mass The two independent examiners never disagreed by more than one point score In those cases the mean score was chosen

The upper two thirds of the right femur were removed and stored in formol 4 % The specimen was then placed directly on cassette free Agfa Gevaert Osray RPI and exposed in the same a p projection as used in a living subject i e with approximately 15 degrees internal rotation in the hip joint Exposure data were 93 kV 70 mAs 1 m FFD The films were developed in a 90 s machine (Pako—XU) In a preliminary investi ation of 12 cadavers the radiologic appearance of the trabecular bone in the neck of free dissected femora was compared with that of the femora in situ No systematic differences were found In the femora the ratio of the greatest cortical thickness to the total diameter of the shaft at the same level was determined and osteoporosis defined as a ratio below 0 5 (NORDIN 1960)

Results

In 28 of 89 cases (30 %) the Singh index diverged from the subjectively estimated bo e mass of the vertebrae (Fig 2) Of 31 vertebral specimens considered to be osteoporoti only 13 scored a Singh index of 3 or lower Of 58 vertebral specimens esti mated to be of normal bone mass the Singh index indicated osteoporosis (lower than 4) in 10 The poor correlation was also borne out by a low coefficient of linear correla tion r = 0 39 and a low Spearman s coefficient of rank correlation (r = 0 52) Because

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APPEARANCE OF TRABECULAR BONE IN THE FEMORAL NECK (SINGH INDEX)

Relation to vertebral bone mass post mortem

A DISEN, H M FREY R LANGHOLM and T VÅGSLID

It has been stated by SINGH et coll (1970) that the radiographic appearance of the trabecular bone in the femoral neck reflects the degree of mineralization of trabecular bone in general A satisfactory correlation was considered to exist to the osteoporosis found in iliac crest biopsies at microscopy The trabecular bone in the femoral neck was graded 1 to 6 grade 6 indicated normal bone mass and grade 1 severe osteoporosis (Singh index) It was considered possible to distinguish between individuals with and without vertebral compression fractures due to osteoporosis with an overlap of 10 7 per cent (SINGH et coll 1972) However a direct comparison between the Singh index and vertebral bone mass has not been performed Therefore it was found motivated to compare the vertebral bone mass in 89 post mortem specimens with the Singh index and with the thickness of cortical bone in the femoral shaft The main purpose was to evaluate the reliability of the Singh index in the radiologic diagnosis of early osteoporosis of the spine

Material and Methods

Post mortem radiography was performed on 97 consecutive autopsy cases brought to the Department of Pathology from the surgical and medical departments Cases with disease or trauma located to the inferior extremities were excluded None had

Submitted for publication 5 January 1978

Table

Age and sex distribution

Age (years)	Females	Males
30–40		1
40–50	4	3
50–60	4	7
60–70	7	15
70–80	16	18
80–90	12	8
90–100	1	

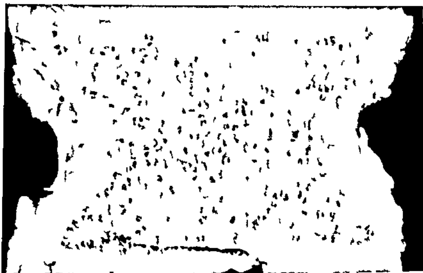
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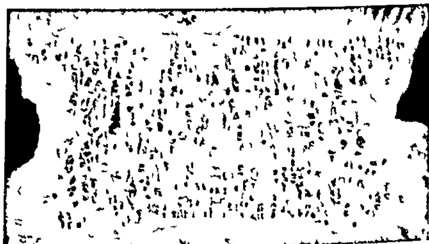
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Results

In 78 of 89 cases (30) the Singh index diverged from the subjectively estimated bone mass of the vertebrae (Fig 2) Of 31 vertebral specimens considered to be osteoporotic only 13 scored a Singh index of 3 or lower Of 58 vertebral specimens estimated to be of normal bone mass the Singh index indicated osteoporosis (lower than 4) in 10 The poor correlation was also borne out by a low coefficient of linear correlation r = 0 39 and a low Spearman s coefficient of rank correlation (r = 0 52) Because



Grade 6. Normal vertebral structure and mass



Grade 3. Moderate osteoporosis. Bone trabeculae reduced



Grade 1. Marked osteoporosis. Slight vertebral compression. Sparse widely separated thin bone trabeculae and cyst formation

Fig. 1. Grading of bone mass. Frontal slices of lumbar vertebrae

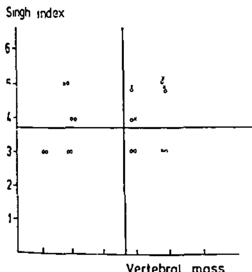


Fig 2 Correlation between vertebral bone mass subjectively estimated and Singh index The lines divide between normal and osteoporotic vertebrae O = females = males

the majority of the osteoporotic cases were not detected by the Singh index its greatest defect seems to be a tendency to underdiagnose the condition

A trend to increasing vertebral osteoporosis in old age exists particularly for females but generally normal bone mass is preserved into very old age (Fig 3 a)

Only 11 cases had a Singh index indicating osteoporosis in the age group above 79 years (Fig 3 b) while in the same age group vertebral osteoporosis was actually present in 25 (Fig 3 a)

The femur index disagreed with vertebral bone mass in 29 of 89 cases (Fig 4) The merit of this index therefore is not better than that of the Singh index

Discussion

One weakness of the present investigation is the absence of objective criteria for vertebral osteoporosis The same objection is however also relevant to the original work of SINGH et coll (1970) They did not use vertebral bodies but iliac crest biopsies where the degree of osteoporosis of cancellous bone was assessed subjectively by visual inspection of magnified photographs The subjective evaluation of the degree of bone rarefaction in the present material was however not difficult neither was the determination of the Singh index With this limitation the correlation of the Singh index to vertebral osteoporosis was so poor that the usefulness of this index in clinical practice is very doubtful Particularly disappointing was the finding that the presence of osteoporosis was underestimated which implies that the index cannot afford the desirable early detection of osteoporosis

The present results agree with those of KRANKENDONK et coll (1972) who found poor correlation of the Singh index with bone mass estimated by ^{125}I photon absorp-

Vertebral mass

a

Singh index

b

Fig 3 Correlation between age and a) vertebral bone mass and b) Singh index Horizontal lines divide between osteoporotic (lower than 4) and normal (4 or higher) index values ○ = females × = males

tiometry of the radius Their results have been critisized by SINGH & RIGGS (1973) on the basis that measurement of peripheral cortical bone possibly does not give a representative evaluation of trabecular bone in the axial skeleton The present results with the femoral cortical index may be taken to support this opinion but the objection of SINGH & RIGGS is not pertinent to the poor correlation between Singh index and vertebral bone mass in the present material

Because the evaluation of osteoporosis in the vertebral bodies is a relative one the abscissa on Fig 2 2 may extend too far to the right i e the presence of osteoporosis in relation to the Singh index may have been overdiagnosed Correcting for this by moving the abscissa to the left thereby increasing the number of vertebral specimens

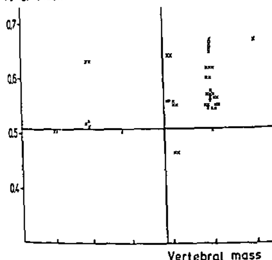


Fig 4 Correlation between vertebral bone mass subjectively estimated and the femoral index The lines divide between normal and osteoporotic vertebrae O = females = males

of normal bone mass would however not alter the main point a vertebral bone mass given a certain Singh index may vary widely and conversely vertebrae with comparable mass may have a widely varying Singh index

Because DALÉN (personal communication) using roentgen spectrophotometry found the Singh index better correlated to age than to bone mass an attempt was made to estimate vertebral bone mass and Singh index in relation to age (Fig 3) In agreement with SINGH et coll (1972) but in contrast to others (EXTON SMITH et coll 1969 JOHNSTON JR et coll 1968 TROTTER et coll 1960) it was found that a large proportion of all individuals maintain normal vertebral bone mass into old age However the statement of DALEN that the Singh index declined more rapidly than vertebral bone mass in age above 70 years was not confirmed

SUMMARY

In 89 consecutive cases trabecular bone mass of the second or third lumbar vertabra was subjectively estimated in post mortem specimens using frontal sections 1 cm in thickness The trabecular appearance of the femoral neck (Singh index) at radiography and the thickness of the femoral cortical bone were also determined Agreement between vertebral bone mass and either of the two radiologic indices was present in only two thirds of the cases and most often these indices underestimated the presence of vertebral osteoporosis The results indicate that neither of these radiologic indices can be used for clinical guidance of the diagnosis of vertebral osteoporosis in the individual case

ZUSAMMENFASSUNG

In 89 aufeinanderfolgenden Fallen wurde die trabekulare Knochenmasse des zweiten oder dritten Lendenwirbels subjektiv an post mortem Praparaten bestimmt wobei frontale 1 cm

dicke Schnitte verwendet wurden Das trabekulare Aussehen des Collum femoris (Singh Index) und die Dicke des kortikalen Knochens des Femurs wurden ebenfalls rontgenologisch bestimmt Übereinstimmung zwischen der Wirbelknochenmasse und jedem der beiden radiologischen Indizes wurde nur in zwei Drittel der Falle gefunden in den meisten der Falle unterbewerteten diese Indizes das Vorkommen einer vertebralen Osteoporose Die Ergebnisse deuten darauf hin dass keiner dieser rontgenologischen Indizes als klinischer Leitfaden fur die Diagnose einer vertebralen Osteoporose im individuellen Fall verwendet werden kann

RESUME

Dans 89 cas consécutifs la masse osseuse trabéculaire de la seconde ou de la troisième vertèbre lombaire a été estimée subjectivement sur des pièces d autopsie en utilisant des tranches frontales d 1 cm d épaisseur Les auteurs ont aussi déterminé radiographiquement l aspect trabéculaire de la tete du fémur (index de Singh) et l épaisseur de la corticale osseuse du fémur Il n y avait une concordance entre la masse osseuse vertébrale et l un ou l autre des 2 indices radiologiques que dans deux tiers des cas et le plus souvent ces indices sous-estimaient la présence d une ostéoporose vertébrale Ces résultats indiquent que ni l un ni l autre de ces index radiologiques ne peut servir comme guide clinique pour le diagnostic d ostéoporose vertébrale dans un cas donné

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FROM THE DEPARTMENTS OF DIAGNOSTIC RADIOLOGY AND OTORHINOLARYNGOLOGY
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FACIAL BONE SCINTIGRAPHY

IV Diagnosis of bone involvement by purulent sinuitis

H F BERGSTEDT C CARENFELT and M G LIND

Bone scintigraphy has been reported to be more sensitive than radiography in detecting bone metastases but the relative amount of false positive results is not always stated (SILBERSTEIN et coll 1973 PAPADIMITRIOU et coll 1974 THRALL et coll 1974 BELLIVEAU & SPENCER 1975 OSMOND et coll 1975 BERGSTEDT & HAVERLING 1978) Other lesions such as those caused by trauma inflammation rheumatic disease may also cause an abnormal accumulation of technetium diphosphonate ($^{99}Tc^{m}$ DP) in the bone tissues affected (TILDEN et coll 1973 DESAULNIERS et coll 1974 GENANT et coll 1974 THRALL et coll KAYE et coll 1975 LETTS et coll 1975 ROSENTHALL & KAYE 1975 GARCIA et coll 1976 LIND & NATHANSON 1977) The exact mechanism of this accumulation of the bone seeking radiopharmaceuticals is not fully known (TILDEN et coll GENANT et coll KAYE et coll ROSENTHALL & KAYE GARCIA et coll) Facial bone scintigraphy has been demonstrated to be of diagnostic value in neoplastic or inflammatory paranasal sinus lesions (BERGSTEDT & LIND 1978)

Presumably the bony walls of the paranasal sinuses are involved in purulent sinuitis although conventional radiography is not sensitive enough to reveal the bone reaction Whether such a bone tissue engagement can be discovered by facial bone scintigraphy was evaluated in a clinical material and the results are now reported

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dicke Schnitte verwendet wurden Das trabekulare Aussehen des Collum femoris (Singh Index) und die Dicke des kortikalen Knochens des Femurs wurden ebenfalls rontgenologisch bestimmt Übereinstimmung zwischen der Wirbelknochenmasse und jedem der beiden radiologischen Indizes wurde nur in zwei Drittel der Falle gefunden in den meisten der Falle unterbewerteten diese Indizes das Vorkommen einer vertebralen Osteoporose Die Ergebnisse deuten darauf hin dass keiner dieser rontgenologischen Indizes als klinischer Leitfaden fur die Diagnose einer vertebralen Osteoporose im individuellen Fall verwendet werden kann

RÉSUME

Dans 89 cas consécutifs la masse osseuse trabeculaire de la seconde ou de la troisième vertèbre lombaire a été estimée subjectivement sur des pièces d autopsie en utilisant des tranches frontales d 1 cm d épaisseur Les auteurs ont aussi déterminé radiographiquement l aspect trabéculaire de la tete du fémur (index de Singh) et l épaisseur de la corticale osseuse du fémur Il n y avait une concordance entre la masse osseuse vertébrale et l un ou l autre des 2 indices radiologiques que dans deux tiers des cas et le plus souvent ces indices sous-estimaient la présence d une ostéoporose vertébrale Ces résultats indiquent que ni l un ni l autre de ces index radiologiques ne peut servir comme guide clinique pour le diagnostic d ostéoporose vertébrale dans un cas donné

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Fig 2 Radiography and scintigraphy in a p projection Patient with purulent maxillary sinuitis

Radiography included 4 standard projections Facial bone scintigraphy was performed with a gamma camera (Nuclear Chicago Pho Gamma IV) 5 h after intravenous injection of 370 MBq (10 mCi) of $^{99}Tc^{m}$ DP A converging collimator was used and 300 000 counts were collected in each projection The skull was examined in a p as well as in left and right lateral projections The inhomogeneity of the gamma camera field was checked at weekly intervals The impurity of the tracer was controlled daily and not allowed to exceed 5 p r cent

Aspiration of secretion from the affected maxillary sinus was carried out within one day after the scintigraphy and radiography The secretions were classified as purulent or non purulent according to CARENFELT & LUNDBERG (1977)

Results

The scintigrams were classified in 4 groups I—definitely normal II—probably normal III—probably abnormal and IV—definitely abnormal All patients in the reference group were normal at radiography and the maxillary regions in the scintigrams were classified as definitely normal (Figs 1 3) In all patients with purulent sinuitis the air of the sinuses was completely replaced by material with the attenuation of soft tissue no bone tissue involvement was demonstrated (Fig 2) All patients with purulent sinuitis had abnormally high uptake of $^{99}Tc^{m}$ DP in the region affected 10 regions were classified as definitely abnormal (group IV) and one as probably abnormal (group III Figs 2 3)

In each patient the $^{99}Tc^{m}$ DP concentration in pus mucosa and bone was divided by the blood concentration giving ratios in the following ranges pus 0 16 to 0 6 ($\bar{x}$ = 0 3) mucosa periosteum 1 1 to 2 3 ($\bar{x}$ = 1 6) and bone 6 6 to 65 ($\bar{x}$ = 26)




Fig 1 Radiography and scintigraphy in a p projection Patient of reference group

Material and Methods

From a material of 25 patients with a suggestion of inflammatory paranasal sinus lesions, examined by radiography and facial bone scintigraphy 11 patients with non aerated maxillary sinus at radiography and purulent inflammation proven by aspiration were selected

Four patients had a history of sinuitis from one to 4 weeks and the remaining patients from one month to about one year

In 4 patients the $^{99}Tc^{m}$ DP concentration in blood and pus was measured by the use of a well counter in samples aspirated 5 hours after the intravenous injection of the tracer

Among the 11 patients 4 had the affected maxillary sinus explored by operation 3 to 4 hours after an intravenous injection of $^{99}Tc^{m}$ DP Bone pieces from the anterior and medial walls of the sinus were dissected free from mucosa and periosteum and weighed Samples of blood and pus aspirated at operation and pieces of mucosa including periosteum were also weighed The amount of $^{99}Tc^{m}$ DP in the different specimens was measured in a well counter and after correction for differences in density the $^{99}Tc^{m}$ DP concentration was calculated for bone mucosa pus and blood

Eight patients with mammary carcinoma at an early stage with no paranasal affection or any other disease of the skull constituted a reference group Radiography of the facial region demonstrated no abnormalities and no surgery had been performed in this region

SUMMARY

Facial bone scintigraphy demonstrated bone tissue involvement by purulent maxillary sinuitis in 11 patients examined In no case was bone involvement demonstrated by radiography Bone scintigraphy in this respect appears more sensitive than does conventional radiography

ZUSAMMENFASSUNG

Die Gesichtsknochen Szintigraphie zeigte eine Beteiligung des Knochengewebes bei einer purulenten maxillaren Sinuitis bei 11 untersuchten Patienten Bei keinem der Falle war eine Knochenbeteiligung durch die Rontgenuntersuchung nachweisbar Die Knochenszintigraphie erscheint in dieser Hinsicht empfindlicher als die konventionelle Rontgenuntersuchun zu sein

RESUME

La scintigraphie osseuse faciale a montre une atteinte du tissu osseux au cours de la sinusite maxillaire purulente chez 11 malades examines Dans aucun de ces cas l atteinte osseuse n était mise en evidence par la radiographie La scintigraphie osseuse a cet egard parait plus sensible que la radiographie simple

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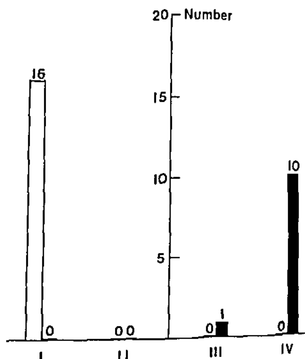


Fig 3 Actual maxillary sinus region at scintigraphy I—Definitely normal II—Probably normal III—Probably abnormal IV—Definitely abnormal White columns Reference group of 8 cases 16 maxillary sinuses Black columns 11 cases with purulent maxillary sinuitis 11 maxillary sinuses

Discussion

The evaluation of bone scintigraphy is based on the uptake of $^{99}Tc^{m}$ DP in bone tissues the mechanism of which is not known in detail The diagnostic capacity of bone scintigraphy in relation to radiography in separating normal bone tissue from bone tissue involved by neoplastic or inflammatory lesion is not definitely established

Purulent maxillary sinuitis evidently affects the surrounding bone tissue Facial bone scintigraphy with $^{99}Tc^{m}$ DP demonstrated definitely abnormal high uptake in the region affected although bone tissue involvement was not demonstrated at radiography The concentration ratios calculated for pus mucosa periosteum and bone in relation to blood demonstrate that the abnormally high concentrations of the tracer in the maxillary regions affected cannot be explained by an increased concentration of $^{99}Tc^{m}$ DP in the inflammatory mucosa or periosteum or by an uptake in the pus but only by high concentration in the bone tissue The results indicate that the bony walls of the maxillary sinus are involved by a purulent sinuitis despite the absence of radiographic indication of an osteitic reaction In all probability the sinuitis was of a bacterial origin in these patients the purulent secretion indicating that a significant number of bacteria was involved in the inflammatory process of the sinus (FREDERICK & BRAUDE 1974 CARENFELT 1977 CARENFELT et coll 1977 CARENFELT & LUNDBERG 1978)

It may be concluded that the dynamic evaluation based on the $^{99}Tc^{m}$ DP uptake process has a higher diagnostic capacity in differentiating patients with bone tissue involvement by purulent maxillary sinuitis from normal subjects than does the morphologic evaluation by conventional radiography

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THIN BONY WALLS OF THE TEMPOROMANDIBULAR JOINT

Morphologic properties and tomographic reproduction

O ECKERDAL and J AHLQVIST

The high efficiency of tomography with hypocycloidal movement may provoke exaggerated expectations However as in every system certain limits exist as well as diagnostic traps One way to learn about the limits and hence also to ameliorate the diagnostic skill is to compare the morphology with its tomographic representation This may be reached in several ways One way is to compare the radiographic findings with those obtained at surgery (HARWOOD NASH 1970) Another way is the method of REISNER (1970) He used a total head specimen and prepared defects in different bony walls bordering on soft tissues or air filled cavities A good correlation was found between the thickness homogeneity and angulation of bony walls and their tomographic reproduction Still another method is to systematically section an autopsy material thus covering a broad spectrum of morphologic and pathologic variations in the region of interest (ECKERDAL 1973)

The intention of the present report is to describe the morphologic features of two thin bony walls in the inner third of the temporomandibular fossa and their tomographic appearances The prerequisites for tomographic reproduction of thin bony walls in general is then discussed

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Fig. 2. Transversal section through the temporomandibular joint. The medial part of the roof of the fossa is hour glass shaped with a central thin part. The thin bony wall (→) between the joint and the intracranial space is parallel with an axial plane. In such cases the wall is demonstrated at tomography with evident contours. A false discontinuity may arise if the wall deviates from the axial plane by more than 18°. The false image arises easier if the bony wall is thin.

enamel paper. The precision of the evaluations was enhanced by enlargement. The first bony wall estimated separated the middle ear and the temporomandibular fossa and was measured in its thinnest part. This wall is almost perpendicular to a sagittal plane and has only a very slight curvature. It has an orientation identical with that of the tympanic bone and constitutes an immediate continuation of this bone. The second bony wall estimated was the roof separating the medial part of the temporomandibular fossa from the intracranial space. This part is often spheric and may also be angulated in relation to an axial plane of the skull (Fig. 2). The morphology of these two bony walls was correlated with the tomographic image.

Results

Morphologic appearances. The dimensions of the bony wall separating the temporomandibular joint from the middle ear are given in the Table. The wall had an even thickness and was relatively large; its vertical dimension appears in Fig. 3 a–d. Only small structural differences were found in this thin bony wall, consisting of cortical bone only.

The thickness and shape of the roof of the fossa varied widely (Table). A transversal section of the roof may be described as hour glass shaped (Fig. 2). The thin central part of this "hour glass" was small compared with that of the bony wall in the anterior part of the middle ear (Fig. 3 a–d).

The tomographic reproduction of the two bony walls differed. In lateral tomographic sections morphologic details and dimensions of the bony wall separating the temporomandibular fossa and the middle ear were reproduced with high accuracy. Even small discontinuities were with few exceptions clearly demonstrated (Fig. 3 e–h).

The accuracy of tomography of the medial part of the roof of the fossa was considerably lower. The morphology was correctly reproduced in some cases but in others erroneous images occurred, giving an impression either of a thickened wall or a loss of bone which sometimes simulated a perforation to the intracranial space.

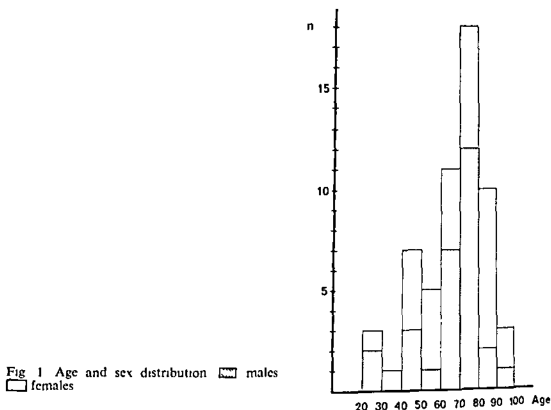


Fig 1 Age and sex distribution ▨ males
☐ females

Material and Method

The material comprised 58 autopsy specimens (29 males 29 females) consisting of the temporal bone and the proximal part of the mandible Age and sex distribution appears in Fig 1 The specimens were chosen at random during a 6 year period Cases with known developmental disturbance were excluded The specimens removed en bloc, were deep frozen embedded in carboxy methyl cellulose and frozen in a mixture of dry ice and hexane (ULLBERG et coll 1971) The blocs were tomographed and sectioned in a microtome in corresponding sagittal layers (ECKERDAL 1973) The Polytome (Philips Massiot) with hypocycloidal movement was used nominal focal size 0 6 mm × 0 6 mm exposure 6 s at 53 kV and 25 mA Siemens Saphir intensifying screens and Kodak RP film were used Microradiography of the specimens was performed using the technique previously described by ECKERDAL (1972) The anatomic details in the tomographic sections the microradiographic images and histologic slides of 20 μm microtome sections were related to each other with the aid of a three dimensional orientation system (ECKERDAL 1973) The calculations were performed on a continuous series of sagittal morphologic sections separated by one millimeter

The microradiographic images and sometimes as a supplement the histologic sections adhered to the collulose tape were projected and enlarged in a Werth Profile projector Record 72 the enlargement factor chosen was 20 The morphologic contours projected on the ground glass table of the projector were traced on transparent

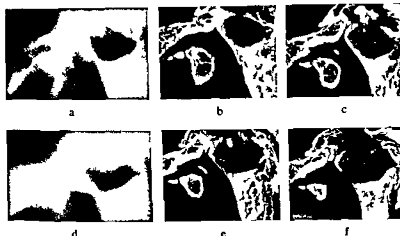


Fig 4 a d) Tomographic images separated by 2 mm and situated on each side of the tympanic membrane b c e f) Microradiography separated by 1 mm demonstrating the posterior wall of the temporomandibular joint The tomographic sections in (a) and (d) correspond to the morphologic layers in (b) and (e) The bony wall is extremely thin in (e) and (f) These layers are separated by 1 mm from layer (c) with its thick wall An insufficient blurring of the laterally thicker wall (b) and (c) explains the discrepancies between morphology and tomographic image in (d)

occur was low despite the fact that the wall was found to be extremely thin $\bar{x}$ 0 6 mm However as demonstrated in Fig 4 difficulty may arise in demonstrating a thin part of the bone In this case it was due to the fact that the thin part had a small extension (Fig 4 e f) and that a dominating thick wall was present in adjacent layers (Fig 4 b c) Fig 4 c and e are separated by one mm which illustrates a lack of layer selectivity of the tomograph

In a lateral projection the wall between the middle ear and the temporomandibular joint is practically perpendicular to the tomographic table The distance to the high attenuating base of the skull is as great as to permit an effective tomographic blurring This fact allows a correct reproduction even of subtle morphologic contours in the tomographic sections (Fig 3 e–h) The more laterally situated tympanic bone is parallel with the actual wall The thickness of the two walls does not differ significantly in the vicinity of the middle ear These morphologic features contribute to explaining the well depicted contours of the actual bony wall as well as the high dimensional accuracy Finally the air filled middle ear and auditory canal ameliorate the tomographic blurring and give a high contrast Representative tomographic and microradiographic image sequences are demonstrated in Figs 3 to 5

The topographic relation between the temporomandibular joint and the middle ear makes it easy to consider an inflammatory process in the middle ear as a possible etiologic factor to arthritis (ARNAUDOW 1967) In case of a unilateral arhtritis the otologic history must be analysed

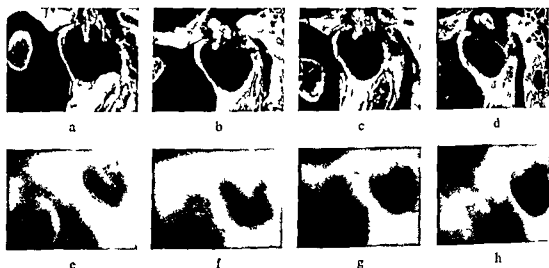


Fig 3 The bony wall separating the temporomandibular joint and the middle ear cavity a–d) Microradiography from different specimens demonstrating various thicknesses of the wall The structure of the cortical bone is almost homogeneous e–h) Tomographic reproductions

Discussion

The difference in accuracy in the tomographic demonstration of the two thin bony walls x 0 6 and $\bar{x}$ 1 1 mm respectively representing a common morphologic feature (a thin well defined cortical bony wall bordering on soft tissue or an air filled cavity) defines to some extent the possibilities and limitations of hypocycloidal tomography The differences in reproduction may be ascribed to technical conditions the projections used or to individual variations of the morphology The influence of the first factor may be considered as standardized and equal in the present series the latter two are thus of main interest

The wall separating the middle ear and the temporomandibular joint was in a true lateral projection reproduced with a high degree of accuracy the tomographic image and the morphologic section corresponded The probability that a false image should

Table

Calculation of the dimensions of two thin bony walls in the medial third of the mandibular joint cavity The measures are given in millimeters

	Total group n = 58			Males n = 29			Females n = 29		
Morphologic part	$\bar{x}$	S	Range	$\bar{x}$	S	Range	$\bar{x}$	S	Range
Roof of the fossa	1 14	0 87	0 08–3 62	0 96	0 75	0 14–3 63	1 32	0 98	0 08–3 03
Wall between middle ear and joint	0 59	0 43	0 12–1 80	0 62	0 45	0 00–1 62	0 56	0 42	0 00–0 80



Fig 6 a) False tomographic image of the roof of the temporomandibular fossa The discontinuity perceived is due to a thin bony wall which is slightly bent and also angulated in relation to an axial plane False images of this kind may be considered as real b) Tomographic image of a penetrating destruction of the roof of the fossa The process is combined with a marginal sclerosis (confirmed by biopsy)

tion of 48 when the hypocycloidal movement is used According to REISNER the critical reproduction limit would be 24 but it is often lower in the temporomandibular fossa (ECKERDAL 1973)

The influence of the angulation on the tomographic image of these thin bony walls is illustrated in Fig 5 The extremely thin bony wall in the roof (Fig 5 a) is reproduced (Fig 5 c) but due to insufficient blurring of the angled roof the bone seems to be thicker than in reality On the other hand when the wall as the posterior one is e tmally angled its dimension in the specimen and in the tomographic image is similar (Fig 5 a–d)

A common feature at tomography of this part of the joint in lateral projection is a false bony discontinuity in the roof at the fossa (Fig 6 a) This depends on a combination of the thin bony wall and a steep angle of the bony surface This may exceed the limit of the tomographic reproduction The positioning of the patient may also interact with the angulation

If it in a special case is of diagnostic importance to demonstrate with certainty the existence of a bony wall between the intracranial space and the temporomandibular joint, this necessitates a positional angle correction in the lateral projection The medial roof of the joint has to be parallel to or at least form a small angle (0–10) with perpendicular to the tomographic table An a p projection with a tomographic section in the central part of the fossa may also be used

The reproduction of the actual bony contours will also be affected by unfavourable blurring conditions Representative tomographic and morphologic images of this region with and without discontinuity appear in Figs 5 and 6

Severe defects in the fossa are not frequent Only few reports have appeared concerning traumatic perforations of the medial roof of the fossa and hence also a communication between the joint and the intracranial space (HORNE 1963) In such cases the condyle may be dislocated intracranially Inflammatory lesions do not tend to break through the roof Cases have been described indicating that a destructive bony lesion is compensated for by bone apposition intracranially

At this department only one case with a communication to the intracranial space has been found in 10 years (Fig 6 b) The tentative diagnosis was synovitis villosa The great majority of bony discontinuities in the medial part of the temporomandibular joint found at tomography in the lateral projection appear to be false (Fig 6 a)

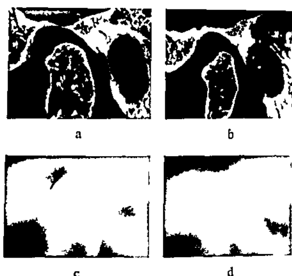


Fig 5 a b) Specimen with extremely thin bony wall The distance between the layers is 4 mm c d) Corresponding tomographic sections The thin bony roof in (a) is masked or seems to be thicker in the tomographic image (→) depending on the angulation and insufficient blurring of surrounding more voluminous parts of the hour glass shaped roof

The bony wall constituting the roof of the temporomandibular joint has another appearance and position which influence the tomographic reproduction Thus the thickness of the roof of the fossa may often be inexactly reproduced The hour glass shape of the actual part of the roof is less favourable to demonstrate than the almost parallel contours of the wall between the middle ear and the temporomandibular joint The thin part of the roof may not be demonstrated depending on lack of layer selectivity of the hypocycloidal tomograph (Fig 5 a c) In the layer which is illustrated in Fig 5 a and c a discrepancy exists between the morphology of the roof and the fossa and its tomographic image This image presents a roof which is thicker than in reality However only the inferior outline of the broad image of the roof represents the true bony wall Sometimes distant high attenuating skeletal parts, even the mandibular condyle (ECKERDAL 1973) may interfere with the reproduction (Fig 2)

The often spheric appearance of the roof of the fossa and the angulation in relation to an axial plane may be as great as to exceed the limit of tomographic reproduction in the lateral projection This limit was by ECKERDAL (1973) found to be individual A false discontinuity would for example appear at 18 in one patient and at 28 in another due to the influence from adjacent skeletal details affecting the tomographic image in the individual case

A thorough analysis of the reproduction of different types of bony walls and well specified defects in them was made by REISNER The present experimental conditions resemble those of REISNER He found a reproduction limit of defects in angled bony walls up to 15 if the wall was very thin 20 to 30 when it was thick (3 mm) The reproduction of defects in a bony wall may to some extent be used as a criterion of quality as concerns the demonstration of the wall per se in the tomographic image REISNER concluded that the reproduction limit may be deduced from the tomographic angle which in this calculation should be divided The Polytome has a total angula

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INFLUENCE OF RADIATION DOSE ON IMAGE QUALITY

S REICHMANN and K ÅSTRAND

Traditionally radiographic image quality has been considered to be limited by certain physical factors operating more or less independently of each other One such factor is unsharpness caused by the finite size of the focus motion of the object and spread of light within the screen film system (MORGAN 1962) Another important factor is the background mottle which stems mainly from the quantum mottle of the radiation relief (ROSSMANN 1964) The depiction of objects of small extent in a plane parallel to the film and yet with a high absorption difference in relation to its surroundings has been considered to be limited mainly by unsharpness (ROSSMANN 1966) In clinical radiography these conditions are very rare objects of small dimensions usually having a low absorption difference in relation to their surroundings Such objects are instead limited by noise as well as by unsharpness (ROSSMANN 1966)

The background mottle increases when the sensitivity of the recording medium is increased In modern high speed radiography the background mottle imposes impairment of image quality in what way the noise impairment of the quality operates when the sensitivity of the recording medium is changed is discussed in the present communication The background mottle caused by random fluctuations of roentgen photons is inversely proportional to the square root of the number of photons per unit area (ALBTECHT & OOSTERKAMP 1962) This means that if the speed of the recording medium is increased by a factor 2 then the background mottle will be increased by a factor 1 4 This increase may not appear to be very serious in view of the speed gained Furthermore if the speed change is caused by using screens of

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SUMMARY

The morphology of two thin bony walls in the medial third of the mandibular fossa is described on the basis of successive microtome sections of undecalcified temporomandibular joint specimens The requirements for reproduction of thin bony walls at tomography with hypocycloidal movement are defined and discussed

ZUSAMMENFASSUNG

Die Morphologie der zwei dunnen Knochen Wanden im medialen Drittel der Fossa mandibularis wird auf der Basis von sukzessiven Microtom Schnitten des nicht dekalcifizierten Kiefergelenks beschrieben Die Forderungen zur Reproduktion der dunnen Knochen Wande bei der Tomographie mit hypozykloidaler Bewegung werden definiert und diskutiert

RESUMÉ

En se basant sur des coupes séquentielles au microtome d articulation temporo maxillaire non décalcifiée les auteurs décrivent la morphologie de deux fines parois osseuses dans le tiers moyen de la fosse mandibulaire Ils definissent et etudient les conditions permettant d obtenir l image de ces fines parois osseuses en tomographie avec mouvement hypocycloidal

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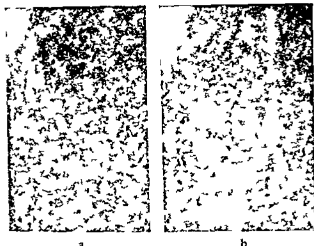


Fig 1 Films of a vessel phantom Magnified details The images were obtained in such a way that unsharpness, contrast and background quantum mottle are identical Still the phantom was recorded in (a) by a dose only 50 of that in (b) If the background mottle had been the only dose-dependent factor with regard to image quality the two images would have been identical However a clear difference exists indicating a noise besides the background mottle

magnified and recopied onto the same film (N 33) In this case two magnified films were obtained from each primary copy In one of them the vessel phantom was depicted In the other only the background mottle appeared the view field area being located beside the image of the vessel phantom Before inspection the films were superimposed in pairs Thus the mottle image from the Curix film was placed on top of the vessel image from the X omatic G film while the mottle image from the X-omatic G film was placed on top of the vessel image from the Curix film This procedure was designed to lead to identical background mottle for the two images in spite of the exposure difference of the vessel phantom itself Since recordings were made with the same screens under constant radiographic conditions and with identical contrast the films should be expected to yield the same image if the influence of photon number on image quality were only a matter of background mottle However in the case where the vessel phantom was depicted with a larger dose more information was evident in the superimposed image (Fig 1) Thus the reduction of exposure had given rise to an impairment of image quality besides that of increased background mottle

In order to define in what way the information was lost in the image obtained with the lower radiation dose the following simulation was performed A Hewlett Packard 9100 B with a plotter was programmed to cover a paper surface with black spots in a completely randomised fashion The number of points to be distributed over a given surface could be chosen so that the covering was performed in steps ranging from 3 200 to 51 200 the increase being made by a factor of 2

higher sensitivity, a certain increase in unsharpness may be expected so that part of the increased background fluctuations will be blurred The increased unsharpness and mottle will to a certain extent eliminate each other, although often encountered this is rarely pointed out in the literature Thus the replacement of ordinary screens by high speed screens would just imply a small but insignificant increase in unsharpness and noise resulting in almost the same image quality even though the speed of the system is increased

However, the problem may be considered in a somewhat different light Each roentgen photon constitutes a carrier of information If the system speed is increased by a factor 2, the number of information carriers is thus decreased to 50 per cent of the original number This would also imply that the total information of the object is reduced to 50 per cent of the original unless the efficiency of the high speed recording medium is higher than that of the low speed one If this is the proper way to view the problem image quality should be expected to deteriorate more rapidly at a given increase in system speed than would be the case if only the background mottle is considered Thus either the reduction of image information is dependent on the square root of the photon number or it is a directly linear function of that number The following experiments were designed to indicate which alternative is the proper one

Experiments

A vessel phantom was exposed The intention was to produce two images of the same phantom where the films would display identical unsharpness contrast and background mottle and yet one image would be obtained with half the radiation dose used for the other image For this reason only one type of screen (Kodak X omatic Regular) was used films being produced by the same pair of screens To achieve the difference of exposure differently sensitive films were used viz Agfa Gevaert Curix RP 1 and Kodak X omatic General When the latter film was exposed the settings of the generator used for the Curix film were kept unchanged the exposure being released twice In this way tube potential (60 kV) as well as focus dimensions (nominal focus 0 6 mm × 0 6 mm) were kept constant In the view field a step wedge was inserted together with the vessel phantom so that the contrast of the two films could be controlled at densitometry Both films were developed in a Pakorol machine in Agfa Gevaert G 138 the processing time being adjusted so as to yield films of identical contrast and density This was possible for the mentioned film speed difference Then the two films were contact copied onto Agfa Gevaert N 33 film the two films being machine developed side by side Since the step wedge image was included it was possible to control afterwards that the two copies were of identical contrast The microdensitometric contrast of the two copies was also controlled The image of one small vessel was scanned with a microdensitometer yielding recordings having the same contrast As a final step the two copies were

Figs 2 a and c display a simulated vessel giving rise to 20 per cent attenuation the number of image points being 50 per cent lower in c than in a The decrease in image points has resulted in increased background mottle The 20 per cent drop-out of image points where the vessel image is simulated yields a small local noise level increase However it appears that the definition of the simulated vessel image is mainly a consequence of the background mottle Figs 2 b and d depicting the 20 per cent drop-out show that actually the vessel image which consists entirely of this drop-out is also poorly defined owing to a mottle inherent in the attenuation process itself Thus the drop-out image points in themselves displaying statistical fluctuation appear against a background characterized by another statistical fluctuation which is in fact the background mottle that can be measured in the final image If the number of image points is reduced by 50 per cent the background mottle is increased but the mottle of the drop out image points representing the attenuation is also increased by the same factor If each of these mottles is assumed to be inversely proportional to the square root of the image point number the signal will be adversely affected by a factor $\sqrt{2}$ and the background mottle will increase by the same factor The total signal/noise ratio would then be expected to be adversely affected by a factor 2

Discussion

The simple experiments performed indicate that in principle the quantitative information content of a radiographic image varies linearly with the number of roentgen photons giving rise to depiction provided that unsharpness can be left out of consideration This means that when this photon number is lowered each object detail to be depicted is represented by a smaller and smaller drop-out of attenuated photons resulting in an increased attenuation mottle to be demonstrated against an increasing background mottle in the final image In the experiments carried out low absorption differences were used so that the noise level of the attenuation mottle would be different from that of the background mottle However if a high absorption difference is considered all the photons being absorbed by the object detail the attenuation mottle can be disregarded since the definition of the object detail in the image is dependent on the background mottle alone In this situation a dose reduction of 50 per cent would theoretically lead to an impairment of information content amounting only to $\sqrt{2}$ Thus a linear relationship between dose and information content is to be expected mainly for fine image details of low contrast However when the depiction of fine details is to be analysed different high contrast objects e g wire meshes are often used The depiction of metal wires where no attenuation mottle affects image quality gives an unrealistic impression of the information capacity of the radiographic system and provides misleading information about how the image quality is altered when the speed of the system is changed

In the mathematical experiment carried out the ubiquitous existence of secondary radiation was not considered If some of the image points are represented by non

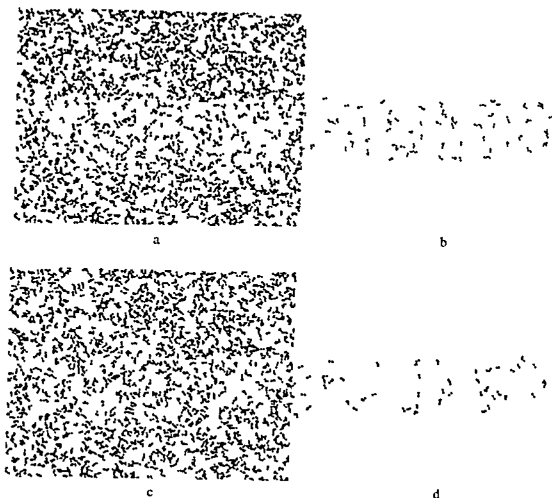


Fig 2 Simulation of the signal/noise ratio in radiography of a vessel Each point represents a photon the distribution of points being randomized The actual films appear in (a) and (c) the exposure of (c) being 50 of that of (a) The vessel represented by a square wave attenuation of 20 appears as a bright band in (a) the signal/noise ratio in (c) being too unfavourable for detection To the right of the vessel image the photons absorbed in the vessel are indicated by (b) and (d) Regardless of background mottle in (a) and (c) the vessel image can never be better defined than is indicated by (b) and (d) The noise of these absorbed photons is the additional noise demonstrated in Fig 1

A sharp depiction of different background mottles was thus obtained Furthermore the depiction of four vessels was simulated These vessels were represented by straight zones of increasing width running parallel across the image Increasing width of the zone also entailed increased attenuation so that the simulated vessel of the greatest calibre represented an attenuation of 25 per cent the corresponding figure for the finest vessel being 10 per cent The attenuation was kept constant for each simulated vessel regardless of the total number of image points Apart from these images, where the vessels were depicted by means of a decreased number of image points seperate images were also made illustrating the number and distribution of the image points representing the randomly absorbed photons (Fig 2)

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EXCRETION OF METRIZAMIDE (AMIPAQUE) IN HUMANS FOLLOWING LUMBAR SUBARACHNOID INJECTION

P AMUNDSEN H WEBER L HOEL and K GOLMAN

Water soluble contrast media when injected intrathecally pass into the blood circulation The major part is excreted via the kidneys small amounts in the faeces No long term investigation seems to have been made of the excretion following subarachnoid application

GOLMAN (1973) in laboratory experiments with metrizamide in rabbits rats and cats recovered 97 to 98 per cent in the urine and faeces 48 hours after injection into the cisterna magna The elimination from the subarachnoid space of different contrast media in clinical use was compared by HINDMARSH (1975) He found that contrast medium could be demonstrated radiologically in the renal pelvis 2 hours after the lumbar injection of methiodal sodium but not after metrizamide injection In one patient injected with methiodal sodium all the medium was recovered in the urine within 24 hours In one patient examined with metrizamide 96 per cent was recovered in the urine during the same period

SKALPE et coll (1973) recovered a mean of 72 per cent of the injected iodine 21 to 24 h after the lumbar injection of 10 ml of metrizamide 170 mg I/ml and SPECK et coll (1978) 73 ± 19 per cent of the contrast media (Amipaque Dimer X and Myelografin) 24 h after the lumbar injection of 10 ml 170 to 140 mg I/ml

From the Departments of Neuroradiology (Director P Amundsen) and Neurology (Director J Presthus) Ullevål Sykehus and the Clinical Department (Director K Dahlstrom) and Research Department (Director U Blix) Nyegaard & Co Oslo Norway Submitted for publication 9 September 1978

LUNGENFUNKTIONSDIAGNOSTIK MIT RADIONUKLIDEN By N Konietzko 97 pages with 50 figures and 17 tables G Fischer Verlag Stuttgart 1977 Price DM 58

This is a clear and concisely written account of the subject going as much into details as reasonably can be expected on the space available The first 50 pages give a short description of radiopharmaca apparatus and methods used in the field and are the best in the opinion of the reviewer On the remaining 35 pages the most important basic facts and concepts of pulmonary physiology and pathology as measured with the radionuclide technique can barely be mentioned Deeper analysis or indication of problems is obviously out of the scope of the author However the closing 12 pages full of references enable the interested reader to pursue the topic further and contribute substantially to the value of the book

Alfred S amosi

Table 2

Dose (mg I) of contrast medium injected into the subarachnoid space

Case No	1	2	3	5	6	8	9	10	11	12	x
Contents of container	1 807	1 807	1 807	1 807	1 807	1 807	1 807	1 807	1 807	1 807	1 807
Residue	443	373	475	322	322	444	494	466	463	242	405
Dose	1 364	1 434	1 332	1 485	1 485	1 363	1 313	1 341	1 344	1 565	1 402

Table 3

Experiment in vitro

Amount injected (ml)	mg I/ml injected	mg I total inj	mg I in container	mg I in syringe	mg I in filter etc	mg I total
9 66	16[illegible]	1 582	70	11	190	1 853
9 8[illegible]	166	1 638	25	12	107	1 78[illegible]
9 850	166	1 635	34	7	109	1 785
9 9[illegible]0	169	1 678	22	7	103	1 810
10 056	165	1 659	12	6	99	1 750
9 708	166	1 612	76	11	113	1 812

excluded) After the examination the patient was kept in bed until the next day the head end of the bed being elevated about 15 degrees for the first 3 to 8 hours

Specimens of urine and faeces from the day and night before the examination were collected for baseline values During 7 days following the examination 24 h specimens of urine and faeces were collected from each patient Two patients (Nos 4 and 7) were excluded because of mishap

The contrast medium remaining in the injection set and the container was calculated spectrophotometrically (JACOBSEN 1972) and the amount of medium injected into the subarachnoid space was calculated by subtracting the residue from the original content of the container (Table 2) If a container of 3 75 g metrizamide is used the exact concentration of the dose cannot be determined as too small an amount of medium remains in the container Moreover the volume injected could only be calculated not measured In order to determine the concentration and to exclude the possibility of non observable leakage during injection a series of in vitro tests were performed Using metrizamide prepared by the same nurse who assisted throughout the clinical series 3 injections were made into a tube by a radiologist participating in the clinical series and 3 by another radiologist well acquainted with the myelographic technique The residue in the container and the injection set was analysed spectrophotometrically as in the clinical series The concentration of iodine (mg I ml) was measured using a refraction index The volume in the tube (dose injected) was calculated from the weight and the concentration The residue was analysed each item separately i e the container injection syringe micro-filter connecting tube and needle (Table 3) The concentration varied from 162 mg I/ml to 169 mg I ml

Table 1

Review of the 12 patients (Nos 4 and 7 failed to fulfil the criteria for the experiment)

Case No	1	2	3	4	5	6	7	8	9	10	11	12
Age (years)	26	20	57	45	47	31	29	25	46	45	16	47
Sex	F	F	F	M	F	F	M	F	F	F	F	F
Body weight (kg)	62	57	75		60	77		68	71	70	60	66
Height (cm)	172	167	161		166	195		185	180	185	170	170
Radiologic diagnosis	Left L4–L5 Disc herniation	Right L3–L4 Disc herniation	Left L5 S1 Disc herniation		Left L4–L5 Disc herniation	Root cysts		No abn	No abn	No abn	Left L5 S1 Disc herniation	No abn

Material and Methods

Twelve patients subjected to myelography because of sciatica were selected All were otherwise healthy adults and all agreed to cooperate The age body weight height and radiologic diagnosis are given in Table 1 All 12 were kept in hospital for at least 7 days after the myelography One patient (No 3) had undergone lumbar myelography 8 days previously Another (No 2) had been operated upon elsewhere for lumbar disc prolapse probably without myelography None of the other patients had a history of previous examination with an iodinated contrast medium or of spinal operation

The myelography was carried out according to the routine technique of the department The patients fasted for 12 to 14 h before and one h after the myelography Lumbar puncture was performed in the lateral decubitus position in a space between L1 and L4 using a 22 gauge (OD 0 72 mm) needle After pressure recording about 4 ml of cerebrospinal fluid was withdrawn for analysis of the iodine content (baseline estimation) A further 5 ml was withdrawn for routine laboratory tests The contrast medium was prepared by dissolving metrizamide 3 75 g (0 48 g I/g) in 8 9 ml of a solution consisting of sodium bicarbonate 5 mg in 100 ml of water using the original metrizamide container Theoretically this provides a volume of 10 6 ml and a concentration of 170 mg I/ml Then 10 ml was withdrawn into a disposable syringe and injected via a connecting tube and a micro filter (Millex 0 22 μm) The container cannula used to fill the syringe connecting tube filter and puncture needle were kept for analysis of the contrast medium that remained

A p and lateral films were exposed with the patient in the prone and both lateral decubitus positions Then the couch was tilted to allow the contrast medium to flow into the conus area in both lateral positions and additional films exposed In 8 patients the contrast medium reached the lower thoracic region in one the middle and in one the upper thoracic region (the 2 patients not completing the experiments

Table 7

Recovery of iodine (mg) from the faeces during the first 7 days after myelography

D	Case No											
	1	2	3	5	6	8	9	10	11	12	x (range)	x ( )
1	—	—	11	—	—	—	—	—	—	—	11 (0–11)	0 7
	—	—	18	—	—	—	40	[illegible]3	7	17	21 (7–40)	1 5
3	—	23	15	—	1	17	—	5	—	—	12 (1–23)	0 9
4	11	—	7	35	3	8	9	11	21	—	13 (3–35)	0 9
5	7	—	4	[illegible]4	7	3	7	6	18	39	13 (3–39)	0 9
6	—	6	4	5	—	3	3	2	5	—	4 (4–6)	0 3
	[illegible]	—	—	—	—	3	1	—	—	12	4 (1–1[illegible])	0 3
Total	[illegible]0	[illegible]9	59	64	11	34	60	47	51	68	44 (11–68)	3 [illegible]

Table 8

Total amount of iodine (mg) recovered from the urine (per cent of total recovered during the first 7 days after myelography) Percentage given in parentheses

	Case No									
	1	[illegible]	3	5	6	8	9	10	11	12
1	669 (53)	463 (49)	894 (59)	534 (59)	429 (57)	142 (1[illegible])	811 (73)	858 (76)	775 (68)	811 (52)
	371 ([illegible]9)	305 (33)	308 ([illegible]0)	186 ([illegible]0)	1[illegible]4 (17)	768 (67)	238 (22)	186 (16)	194 (17)	658 (4[illegible])
3	103 (8)	87 (9)	1[illegible]4 (8)	13[illegible] (14)	1[illegible]6 (3)	12[illegible] (11)	32 (3)	51 (5)	103 (9)	48 (3)
4	4[illegible]	38	26	31	[illegible]0	63	1[illegible]	18	37	23
5	6	17	150	10	24	18	7	13	[illegible]0	11
6	45	1	12	14	16	16	5	7	9	6
7	8	7	7	5	11	15	3	4	7	5
Total	1 [illegible]64	938	1 5[illegible]0	912	7[illegible]0	1 144	1 108	1 136	1 145	1 [illegible]6[illegible]

Table 9

Percentage recovery of iodine excreted recorded for the 7-day period

	Case No									
	1		3	5	6	8	9	10	11	12
Total in urine	9[illegible] 7	65 5	104 9	61 5	50 5	83 9	84 9	84 5	84 6	99 7
Total in faeces	1 4	[illegible]1	4 4	4 3	0 7	[illegible]4	4 6	3 5	3 8	4 4
Total excreted	94 1	67 6	109 3	65 8	51 [illegible]	86 3	89 5	88 0	88 4	104 1

source in the concentration range of 1 to 10 μmol I/l Further testing of the method when using metrizamide as an iodine source confirmed these results (Table 4) In addition to iodine determination the daily urine creatinine excretion was recorded using the reaction of Jaffe (BARTELS et coll 1972)

Table 4

Recovery of iodine after addition of known amounts to faeces or urine

Aliquot No	Faeces			Urine		
	Iodine before addition (μmol/kg)	Iodine added (μmol/kg)	Iodine after addition (μmol/kg)	Iodine before addition (mmol/l)	Iodine added (mmol/l)	Iodine after addition (mmol/l)
1	0 39	50	46 8			
2				< 0 010	0 394	0 40
3				0 11	0 394	0 46

Table 5

Diuresis in 10 patients during the first 7 days after myelography with metrizamide (ml urine/24 h)

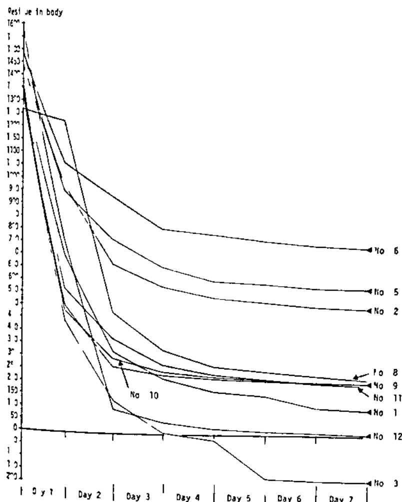
Day	Case No									
	1	2	3	5	6	8	9	10	11	12
1	1 040	1 460	965	1 839	1 557	351	650	1 093	513	473
2	1 218	1 562	1 250	735	907	1 233	971	1 913	457	1 090
3	965	1 597	1 250	1 713	2 260	971	996	2 524	603	1 013
4	1 185	1 893	1 733	1 436	2 556	1 147	1 421	2 537	603	1 368
5	1 885	1 900	1 507	1 056	2 005	885	1 455	2 437	907	1 173
6	773	1 702	1 850	1 579	3 063	1 480	1 090	3 012	740	1 315
7	1 880	1 876	1 739	1 820	2 938	2 237	795	1 529	743	1 599

Table 6

Creatinine excreted (mmol/24 h) during the first 7 days after myelography

Day	Case No									
	1	2	3	5	6	8	9	10	11	12
1	9 3	3 5	12 6	5 8	6 0	4 3	7 8	8 4	8 9	6 3
2	7 8	8 0	11 6	6 2	5 6	17 6	10 4	18 2	6 2	16 6
3	9 3	9 2	9 6	16 4	8 3	12 2	9 8	12 9	10 3	9 4
4	11 4	8 8	3 9	9 1	8 9	14 7	9 7	13 1	8 6	9 4
5	13 0	6 7	8 1	5 8	9 6	16 7	9 8	12 0	11 2	10 3
6	6 5	11 9	8 9	13 7	12 5	12 8	9 8	14 9	10 0	10 7
7	13 6	7 1	7 9	9 0	10 4	28 5	9 9	12 9	9 5	8 8

The specimens of urine and faeces were analysed for their iodine content using a neutron activation method (JOHANSEN & STEINNES 1969 1976) at the Institutt for Atomenergi (Kjeller, Norway) The error of this method has previously been shown to be about 5 per cent when using 3 4 diiodothyronine or l thyroxine as an iodine



Contrast medium (mg I) retained in body Based on the amount in the urine (excretion in the faeces disregarded)

renal function is normal thus considerably simplifying the experimental conditions

More than 70 per cent of the iodine recovered from the urine was collected during the first 48 hours In one patient (No 8) only 12 per cent was retrieved during the first 24 hours but diuresis and creatinine excretion were also low during this period These parameters (and iodine excretion) were unusually high during the second 24 h the 24 h iodine recovery reached 79 per cent The low urinary excretion on the day of examination was probably due to dehydration

During the latter part of the period recovery dropped to only a few mg I/day but even the last 24 h urine contained a measurable content of iodine In all patients

Results

Both the men (Nos 4 7) failed to follow the instructions but all the 10 women collected the specimens of urine and faeces The volume of the urine is given in Table 5 and the creatinine excreted in Table 6

The calculated amount of iodine injected into the subarachnoid space varied from 1 313 to 1 565 mg I (Table 2) The baseline values of iodine in the urine were less than 1 3 mg I/l except in case No 3 who had 2 5 mg I/l For ethical reasons the spinal re puncture originally planned on the 7th day was abandoned and therefore no base line iodine values were determined in the cerebrospinal fluid except in 2 patients In one of these (No 3) lumbar myelography had been performed 8 days before the present examination the other had had no such examination The CSF from case No 3 contained 1 mg I/l that from the other 0 02 mg I/l

The amount of iodine recovered in the faeces and urine appears in Tables 7, 8 and 9 Only 1 4 to 4 6 per cent of the dose i e the contrast medium injected was recovered in the faeces The amount in the urine varied considerably from 50 5 to 104 9 per cent of the calculated dose injected

Discussion

It is well known that the collecting of urine and faeces over a long period is difficult The present patients had been fully briefed and the problem carefully discussed with each Although all were eager to cooperate only the women managed to complete the experiment Even in the successful 10 patients who tried very carefully to follow the instructions some mishap cannot be completely excluded However the figures in Tables 3 and 4 for diuresis and the amount of creatinine excreted do not suggest a loss of urine

The aim was to apply the routine myelographic technique in which a dose of 10 ml of Amipaque 170 mg I/ml is injected The experiment in vitro revealed that the concentration achieved under such conditions differed (between 162 and 169 mg I/ml) This variation must be ascribed to inaccurate dilution with solvent

The dose of contrast medium injected (in mg I) proved to be higher in the in vitro series than in the clinical material This is probably caused by less complete emptying of the tubing under clinical conditions

These results indicate that with the routine myelographic technique the dose is less than 10 ml and the concentration lower than 170 mg I/ml The total injected and the total residue of iodine in the experiment in vitro is well within the accepted variation in the original containers (1 807 mg I ± 5 %) Thus there should be no risk that contrast medium is lost during the injection

The low level of iodine excretion into the faeces in this series agrees closely with the results of animal experiments

In further analysis of metrizamide excretion the faeces may be disregarded provided

RESUME

Les auteurs ont determine l excretion de metrizamide par les reins et l intestin pendant une periode de 7 jours apres l examen chez 10 malades qui avaient subi une myelographie pour une sciatique Au cours de cette periode moins de 5° du moyen de contraste injecte a été retrouvé dans les matières fecales La quantite totale de moyen de contraste retrouvee dans l urine a varie considerablement d un malade a l autre mais la plupart du moyen de contraste a ete excrétee pendant les premieres 48 heures A partir du 4 eme jour les quantite excretees sont petites mais meme le 7 eme jour il restait de 3 a 11 mg d iode ce qui represente de 6 à 22 mg de metrizamide

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except No 3 this content was definitely above the baseline values (<1 mg I/l) In patient No 3 the baseline (2 5 mg I/l) corresponded to the level found in all the patients on the 7th day

The Figure represents a clearance diagram indicating the amount of contrast medium remaining in the body from day to day as expressed by the difference between the iodine injected and the iodine excreted in the urine (The excretion in the faeces has been disregarded in this connection) The individual curves conform fairly well but the residue in the body varies greatly from nearly zero value (No 12) to nearly 50 per cent (No 6) Errors caused by technique could explain minor variations but probably not the wide spread in this material Therefore it must be assumed that after the rapid excretion occurring during the first 2 to 3 days after injection some contrast medium is retained in the body This depot appears to vary individually it is excreted at a low rate and in none of the patients of this series was it completely depleted after 7 days Patient No 3 who had had a lumbar subarachnoid injection of metrizamide 8 days previously, had a depot at the start of the examination and this explains the clearance of over 100 per cent of the dose The iodine level in the cerebrospinal fluid in this patient indicates that at least part of the depot is retained in the central nervous system

Conclusion Only a small amount of metrizamide injected into the lumbar subarachnoid space during myelography is excreted in the faeces—less than 5 per cent Most of the contrast medium is excreted in the urine within 2 to 3 days A small amount remains in the body for more than 7 days being excreted at a slow rate The amount of this retained contrast medium appears to vary greatly from one individual to another Part of it at least is present in the central nervous system

SUMMARY

The excretion of metrizamide through the kidneys and intestinal tract was determined in 10 patients submitted to myelography because of sciatica for a period of 7 days following the examination In the faeces less than 5 per cent of the injected contrast medium was recovered during this period Total recovery in the urine varied considerably from patient to patient but most of the contrast medium was excreted during the first 48 hours From the fourth day on only small amounts were excreted but even on the 7th day 3 to 11 mg iodine remained which corresponds to 6 to 22 mg of metrizamide

ZUSAMMENFASSUNG

Die Ausscheidung von Metrizamid durch Nieren und Darm wurde bei 10 Patienten bei denen eine Myelographie wegen Ischias ausgeführt worden war während einer Periode von 7 Tagen im Anschluss an die Untersuchung bestimmt Weniger als 5 Prozent des injizierten Kontrastmittels wurde durch den Darm während dieser Periode ausgeschieden Die gesamte im Urin gefundene Menge variierte stark von Patient zu Patient aber das meiste des Kontrastmittels wurde während den ersten 48 Stunden ausgeschieden Ab den vierten Tag wurden nur kleine Mengen ausgeschieden aber auch am siebenten Tag wurden 3 bis 11 mg I (6–22 mg Metrizamid) gefunden

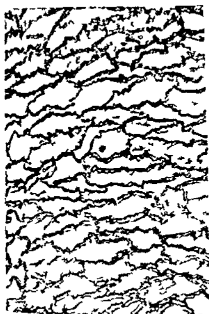


Fig 1

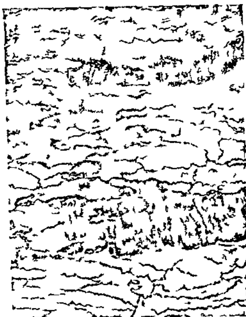


Fig 2

Fig 1 Normal aortic endothelium stained with silver after perfusion with physiologic saline (160)
Fig 2 – Two injured zones with increased endothelial permeability and subendothelial silver lines Perfusion with methylglucamine iodamide solution (160)

The needle was fixed with a ligature when its tip was in the upper part of the abdominal aorta The right half of the thoracic cavity was opened and the heart removed The thoracic aorta was rinsed with 8 to 10 ml physiologic saline A 10 ml test solution was then injected over a 5 min period The vessel was rinsed again with 17 to 18 ml physiologic saline within 45 s after which 5 ml of a 0 25 per cent silver nitrate solution was injected during 30 s followed by 10 ml 5 per cent glucose during 60 s All injections were manual The prefixation of the aorta was performed in situ with a 3 6 per cent formalin perfusion for 30 min The descending part of the thoracic aorta was dissected out carefully Only the most distal and proximal areas of the specimen were touched The ventral wall of the vessel was opened longitudinally and the specimen was fixed by paper tapes on a glass slide with the inner wall facing upwards

The specimens were kept for 22 to 26 hours in 3 6 per cent formalin at −4 C and for 10 to 14 h in distilled water Thereafter they were dehydrated in an alcoholic series for 4 to 5 min in each step and kept for one min in xylene

The specimens were cut beside the tapes placed on glass slides with the inner wall towards and mounted with Permount and cover slips These were kept under pressure until the mounting media had hardened

Light microscopy of the specimens was performed at a magnification of 400 × On one ocular a set of squares was drawn one square covering 1/50th of the field

FROM THE DEPARTMENT OF DIAGNOSTIC RADIOLOGY (DIRECTOR PROF P VIRTAMA)
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ROLE OF HYPERTONICITY IN THE ENDOTHELIAL INJURY CAUSED BY ANGIOGRAPHIC CONTRAST MEDIA

R RAININKO

The property of contrast media to increase endothelial permeability is known and is considered to be one reason for angiographic complications the factors lying behind are however mainly unknown

The osmolality of a solution was considered relatively unimportant by HARRINGTON et coll (1966) but was estimated as a contributing although not the only responsible factor to the endothelial injury by SÖRENSEN (1971) and WALDRON et coll (1974) In some later reports hyperosmolality has been stated to be the only factor in permeability alteration (RAPOPORT et coll 1974 STERRETT et coll 1976)

The effect of increasing osmolality on the permeability of vascular endothelium was measured quantitatively and the effect of some contrast media on the endothelium was compared with that of equiosmolal sodium chloride solutions which were considered to have minimum chemotoxicity The results are now reported

Materials and Methods

The material consisted of 120 white male rats weighing 320 to 400 g The animals were anesthetized with sodium pentobarbital (Nembutal Veterinary Abbott) injected intraperitoneally The peritoneal cavity was opened and the abdominal aorta cannulated with a thick needle inserted in cranial direction distal to the renal arteries

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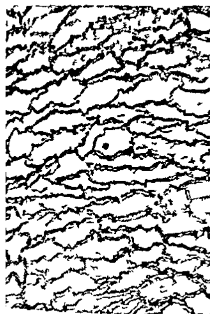


Fig 1

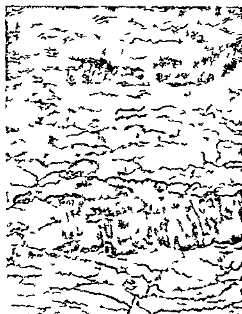


Fig 2

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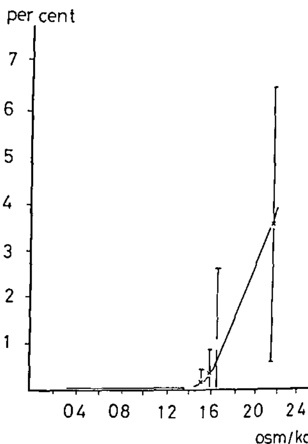


Fig 3 Relation of the percentile injured area of the endothelium to osmolality of sodium chloride solutions The base line values are means ± SD for 10 animals

The areas of endothelial injury were measured using the squares in one hundred or more viewing fields in each specimen The percentile area of the injured endothelium was calculated The areas in which silver had leaked under the endothelium (Figs 1 2) were considered injured For elimination of the effect of possible mechanical injury the marginal areas of the vessel specimen were not measured

Solutions tested Besides physiologic saline 5 solutions containing 44 5 g 48 g 50 g 52 g and 68 g sodium chloride in one kg water were used The osmolalities of the solutions were calculated by the equation

osmolality = m ν Φ where m = molality ν = number of ions formed from one molecule and Φ = osmotic coefficient

The osmotic coefficients at 25 C were taken from the tables given by ROBINSON & STOKES (1959) The osmolalities were 0 3 1 41 1 52 1 59 1 66 and 2 18 respectively

Six contrast media were tested metrizamide (osm 0 46) methylglucamine diatrizoate (osm 1 57) methylglucamine iothalamate (osm 1 54) methylglucamine and calcium metrizoate (osm 1 53) methylglucamine iodamide (osm 1 52) and methyl glucamine and sodium diatrizoate (osm 1 57) The iodine concentration of all contrast media used was 280 mg/ml Distilled water was added if the original commercial

solution was more concentrated The osmolalities of the ionic contrast media were measured at 25 C with a Perkin Elmer 115 Molecular Weight Apparatus with a solution of known concentration of sodium chloride as a reference The method is based on differences in vapor pressures Each contrast medium was tested 6 times and the mean values of the measurements were calculated The osmolality of the non ionic metrizamide is measured by the manufacturer by the same method at 37 C

All solutions were perfused at room temperature 23 to 25 C and each solution was tested in 10 animals

Results

The percentile vascular area in which the endothelial permeability to silver had increased in relation to the osmolality of sodium chloride solution appears in Fig 3 The endothelial injury was almost equal at the level of 0 3 to 1 41 but increased markedly when the osmolality had passed 1 59

The extent of injured areas after perfusion of contrast media and of sodium chloride solutions equal in hypertonicity is compared graphically in Fig 4

The osmolalities of contrast media with iodine concentration 280 mg/ml are at the level where the hypertonicity begins to affect the endothelial permeability except for metrizamide which has a lower osmolality

All contrast media except methylglucamine diatrizoate altered the endothelial permeability more than equiosmolal sodium chloride solution

Discussion

In silver staining of endothelium black granules are deposited in the space between endothelial cells (FLOREY et coll 1959) After endothelial injury silver leaks through the endothelium and dark subendothelial stripes transversal to the vessel appear The injury causing endothelial leakage can be chemical or physical Therefore the mechanical injury should be as small as possible After perfusion with physiologic saline the endothelial injury was only slight which indicates that mechanical injury was relatively insignificant The chemotoxic effect of physiologic saline on the endothelial permeability is also insignificant

The abrupt rise of the curve in Fig 3 after a long almost horizontal part gives reason to assume that besides chemical and mechanical factors another factor affects the endothelial permeability most likely hypertonicity

Osmotic effect on the vascular permeability has previously been investigated in the brain Injury of the blood brain barrier occurs after some electrolyte solutions with similar osmolality which have no specific action on the barrier The injuring effect increases with increasing concentration and the barrier injury is reversible (RAPOPORT et coll 1972) These observations agree with the hypothesis that concentrated solutions open the blood brain barrier by shrinking endothelial cells by

in der Nahe oder uber der osmotischen Schwelle Die meisten angiographischen Kontrast mittel schädigten das Endothel mehr als äquiosmolale Natriumchlorid Losungen Hyper osmolalität ist nur eine der Faktoren die zum Anstieg der endothelialen Permeabilität beitragen

RÉSUME

L effet de l hyperosmolalité sur la perméabilite de l endothélium vasculaire a éte etudié par la microscopie optique et la coloration argentique de l aorte thoracique chez le rat L osmolalité seuil donnant une lesion endothéliale importante a eté de 1 41 a 1 59 deter miné par des solutions de chlorure de sodium Les osmolalités des moyens de contraste ioniques utilisés en clinique ont été égales ou superieures au seuil osmotique La plupart des moyens de contraste angiographique ont lese l endothélium plus que les solutions equiosmolaires de chlorure de sodium L hyperosmolalite n est qu un des facteurs contri buant à augmenter la perméabilité endothéliale

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FROM THE DEPARTMENT OF DIAGNOSTIC RADIOLOGY, ULLEVAAL SYKEHUS, OSLO, NORWAY

AMIPAQUE IN COELIAC ANGIOGRAPHY

A. SKJENNALD

Angiography of the liver and pancreas necessitates large amounts of contrast medium with high iodine content. Such ionic contrast media are strongly hypertonic relative to blood but the toxicity is relatively low.

The water soluble non-ionic contrast medium metrizamide (Amipaque) is in low concentrations (166 mg I/ml) isotonic relative to blood; even in high iodine concentration Amipaque has a low osmolality compared to the ionic contrast media, lower than can be estimated theoretically relative to the iodine content.

It is of fundamental importance for the assessment of pathologic vascularity, particularly in the liver and pancreas, that the small arteries are demonstrated. Theoretically this should be easier with the non-ionic contrast medium.

The purpose of the present investigation was therefore to find out whether the demonstration of small arteries in the liver and the pancreas was improved using Amipaque instead of an ordinary ionic medium. Liver enzymes were determined in each patient before and after angiography in order to evaluate possible differences in toxicity.

Material and Methods

The material consisted of 12 patients aged between 48 and 76 years (mean 56.3 years). 4 patients were examined with Isopaque Coronar (370 mg I/ml) and 4 with Amipaque (3.0 mg I/ml). The position of the catheter, amount of medium and rate of injection were identical in the two groups (Table 1).

In the remaining 4 patients both Isopaque and Amipaque were injected in the coeliac trunk only. In 2 of the patients Amipaque was injected first, in the other Isopaque. An interval between the two injections of 15 min was considered satisfactory for eliminating the influence of the contrast medium first injected upon the

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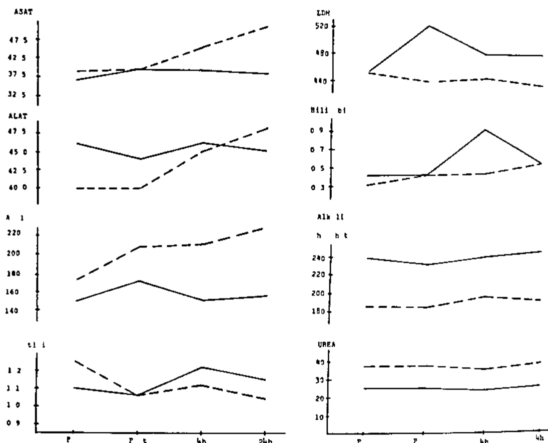


Fig 1 Biochemical enzyme alterations with Amipaque (——) and Isopaque (---) before immediately after and 4 and 24 h after angiography (mean values)

circulation time at the injection of the other medium The injection was performed with an automatic injector A catheter with an end hole and 2 side holes near the tip was used Blood samples were obtained before immediately after as well as 4 and 24 hours after angiography

The arteries in the right liver lobe and the head of the pancreas were drawn on translucent paper and the difference in demonstration of the smallest arteries with the two contrast media was recorded The quality of the venous filling in the 2 series was estimated subjectively on the films The drawings of the arteries and the evaluation of the films were made without knowledge of the contrast medium used The time of maximum arterial filling and initial filling of the splenic vein was estimated for both contrast media The degree of discomfort was also recorded

Results

Neither Amipaque nor Isopaque Coronar caused significant alterations in the biochemical parameters (Fig 1) In all patients Amipaque gave significantly less discomfort than Isopaque (Fig 2)

Table 1

Amount of contrast medium and rate of injection in the different arteries

	Amount (ml)	Rate (ml/s)
Lumbar aorta	30	15
Coeliac trunk	45	12
Common hepatic artery	45	10
Superior mesenteric artery	45	12

Table 2

Time (in s) for maximum arterial filling and initial filling of the splenic vein

Case No	Arteries		Splenic vein	
	Amipaque	Isopaque	Amipaque	Isopaque
1	2 5	1 5	4	3
2	2 0	2 5	6	7
3	3 0	3 0	7 5	6 5
4	4 5	2 5	6 5	6

In the patients examined with both Amipaque and Isopaque maximum arterial filling occurred later with Amipaque in 2 patients earlier in one and in one the time for maximum filling was the same with Amipaque as with Isopaque (Table 2) In 3 of these 4 patients initial filling of the splenic vein was obtained later with Amipaque than with Isopaque (Table 2)

The demonstration of the smallest liver and pancreatic arteries as well as of the veins was improved with Amipaque

Discussion

It is known that angiography with modern tri iodated water soluble hypertonic contrast media does not cause significant biochemical alterations DOUST & REDMAN (1977) observed only a small increase in creatinine in patients who were dehydrated which was normalized the day after examination SKALPE et coll (1973) found only a slight increase in some liver enzymes (ASAT ALAT LDH) the first day after coeliac angiography in rabbits However they used in a single coeliac injection an amount of contrast medium 3 to 4 times as high as in the present cases In these the total amount of medium including the test injections was about 200 ml and no significant biochemical alteration was found It is thus well established that modern contrast media do not cause significant injury to the liver or pancreatic cells at

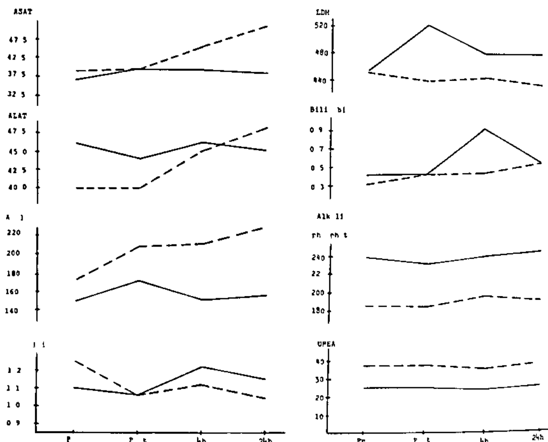


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Results

Neither Amipaque nor Isopaque Coronar caused significant alterations in the biochemical parameters (Fig 1) In all patients Amipaque gave significantly less discomfort than Isopaque (Fig 2)

RESUME

Une angiographie cœliaque a été faite chez 12 malades en utilisant l Ampique à 370 mg I/ ml ou l Isopaque à 370 mg/ml L auteur n a pas constaté de modifications biochimiques importantes dans le serum L Amipaque améliore la mise en evidence des petits vaisseaux dans le foie et dans la tete du pancreas L Amipaque ne cause pas de desagrement a la d fference de l Isopaque qui a donné une sensation de chaleur modérée ou importante au cours de l injection

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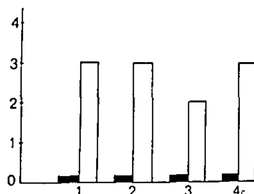


Fig 2 Discomfort of Amipaque (black) and Isopaque (white) 0 = no heat 1 = mild heat 2 = moderate heat 3 = severe heat 4 = intense heat

angiography The reason for the improved filling of small intrahepatic and intra pancreatic arteries and veins obtained with Amipaque could be that Amipaque having a higher viscosity than Isopaque is less diluted in the small vessels than Isopaque The radiographic contrast is hence improved

A hypertonic contrast medium increases the blood flow more than an isotonic contrast medium Therefore an earlier venous filling could be expected with a hyper tonic medium In the present series venous filling was obtained earlier with Isopaque than with Amipaque in 3 of the 4 patients examined with both media The importance of demonstrating the pancreatic veins especially the choledochal vein in the diagnosis of pancreatic carcinoma has been pointed out by UDEN (1976)

At this department Amipaque has been used in superselective angiography with injections into the gastroduodenal dorsal pancreatic and common inferior pancrea ticoduodenal arteries Both the arterial and the venous filling appeared to be improved with the non ionic isotonic contrast medium but the material is at present too small for a final conclusion

The total loss of heat sensation using Amipaque compared to Isopaque corre sponds to other observations (ALMEN et coll 1977 EVENSEN et coll 1977)

SUMMARY

Coeliac angiography was performed in 12 patients using Amipaque 370 mg I/ml or Isopaque 370 mg I/ml No significant biochemical alterations were found in serum Amipaque improved the demonstration of small vessels in the liver and in the head of the pancreas Amipaque caused no discomfort contrary to Isopaque which gave moderate to severe heat during injection

ZUSAMMENFASSUNG

Angiographie der Arteria coeliaca wurde bei 12 Patienten unter Verwendung von Amipaque 370 mg I/ml oder Isopaque 370 I/ml vorgenommen Keine signifikanten bio chemischen Veranderungen wurden im Serum gefunden Amipaque verbesserte den Nach weis der kleinen Gefasse in der Leber und im Pankreaskopf Amipaque rief keine Unbe haglichkeit im Gegensatz zu Isopaque hervor welches massiges bis schweres Warmegefuhl wahrend der Injektion verursachte

Table

Angiographic and microscopic findings in embolized and non-embolized liver tumours

Pair	Embolized rats				Non-embolized rats		
	First angiography	Second angiography	Third angiography	Tumour necrosis	First angiography	Second angiography	Tumour necrosis
1	Tumour	6 days Partial recanalization Decrease in tumour vessels	—	+ + +	Tumour	6 days Increase of tumour size	+ (−)
2	Small tumour	—	—	+ + +	No tumour	—	+
3	Tumours	6 days Tumour supply occluded	—	+ + +	—	6 days Tumour vessels	+
4	Tumours	3 days Tumour supply occluded	6 days Partial recanalization	+ − +	Tumour	6 days Increase of tumour size	− (+)
5	No tumour	2 days Reembolization	4 days Hepatic artery occluded	+ −	Tumours	4 days Increase of tumour size	− (+)
6	Tumours	2 days Reembolization	6 days Partial occlusion with decreased size of tumours	− +	No tumour	No tumour	−

tomy 12 of the rats were grouped in 6 pairs (Table) with approximately the same size and number of tumour nodules in the liver in each pair Celiac angiography (under ether anaesthesia) was then performed using the technique described previously (EKELUND & OLIN 1970 EKELUND et coll 1974) Serial films were obtained in the lateral projection using a small film changer for industrial films (ANGANTYR & OLIN 1973) Following a primary angiography a suspension of Spongostan powder (99 3 gelatin Ferrosan International Denmark) in contrast medium at a concentration of 0 75 mg/ml was injected into the celiac artery in a volume of 0 04 to 0 08 ml during fluoroscopy Then saline was flushed to prevent occlusion of the catheter In each pair of rats this procedure was performed in one rat while its mate was left without embolization Five minutes following embolization repeat angiography was performed to establish the degree of occlusion Prophylactic treatment with penicillin was given to the embolized rats Within 2 to 6 days repeat angiography was performed In 2 rats reembolization was carried out after 2 days In 3 embolized rats a total of 3 angiographies were performed the second catheterization being undertaken from the contralateral femoral artery and the third from the left carotid artery Four pairs of rats were killed on the sixth day after the primary procedure and the

FROM THE DEPARTMENT OF DIAGNOSTIC RADIOLOGY THE INSTITUTE OF PATHOLOGY AND THE WALLENBERG LABORATORY, UNIVERSITY OF LUND S 221 85 LUND SWEDEN

TRANSCATHETER ARTERIAL EMBOLIZATION OF EXPERIMENTAL HEPATIC TUMOURS IN THE RAT

L STIGSSON L EKELUND N JONSSON and H O SJÖGREN

Transcatheter occlusion of the arterial supply of abdominal tumours is receiving increasing interest in clinical radiology (GOLDSTEIN et coll 1976) Major indications include control of hemorrhage palliation of local tumour symptoms and preoperative embolization to facilitate surgery This mode of management has predominantly been applied to renal tumours (ALMGÅRD et coll 1973 GOLDSTEIN et coll) but a few cases of liver neoplasms treated this way have also been reported (DOYON et coll 1974 GOLDSTEIN et coll) It seems important to test the effect of such interventional techniques in experimental models but so far experience with embolization of experimental hepatic tumours appears limited (EKELUND et coll 1977) In the present report the angiographic and histologic findings in a number of embolized hepatic tumours is compared with those in a control group of rats with non embolized neoplasms

Material and Methods

Twenty rats of inbred Wistar/Furth strain each weighing 100 to 200 g were used From a chemically induced rat colon adenocarcinoma (STEELE & SJÖGREN 1974) 3×10^6 living cells were injected into a mesenteric vein through a small abdominal incision and 2 to 3 weeks later explorative laparotomy was performed Three rats with peritoneal carcinomatosis were excluded and another 3 rats died during the experimental period Thus 14 animals remained According to the findings at laparo

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a



b

Fig 2 Same case as in Fig 1 a) 3 days after embolization Partial recanalization of hepatic artery Cranial tumour supply is still occluded while lower tumour is partly revascularized Arterioportal shunting to main portal vein (→) b) 6 days after embolization Catheterization via left carotid artery Revascularization also of cranial tumour Caudal tumour has decreased in size

Autopsy was performed in all 14 animals including a careful macroscopic examination of the liver Multiple sections were prepared from all the livers and stained with hematoxylin-erythrosin and according to van Gieson

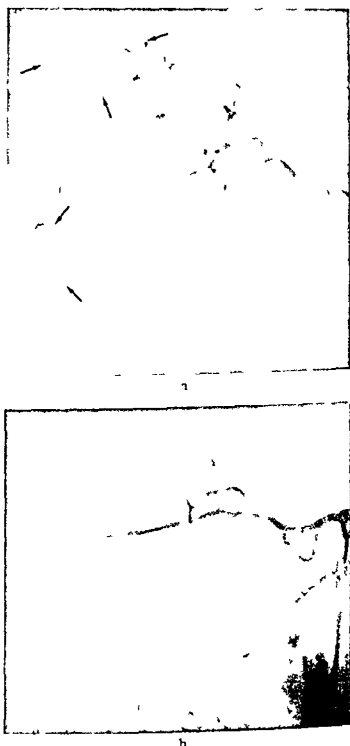


Fig 1 Celiac angiography lateral projection a) Two tumours located ventrally (→) b) 5 min after embolization Hepatic artery branches are occluded and no contrast medium reaches the tumours Reflux of medium to aorta and superior mesenteric artery

remaining pairs on the second and fourth days respectively Finally in the remaining 2 rats with liver tumours embolization was carried out without any controls One of these rats was reembolized after 2 days and the animals were killed after 3 and 8 days, respectively

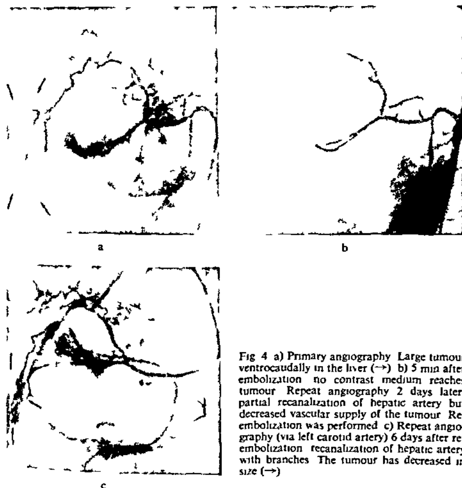


Fig 4 a) Primary angiography Large tumour ventrocaudally in the liver (→) b) 5 min after embolization no contrast medium reaches tumour Repeat angiography 2 days later partial recanalization of hepatic artery but decreased vascular supply of the tumour Re embolization was performed c) Repeat angiography (via left carotid artery) 6 days after re embolization recanalization of hepatic artery with branches The tumour has decreased in size (→)

At angiography 5 minutes after embolization it was demonstrated that no contrast medium reached the tumours and repeat examination always showed partially or totally occluded tumour supply (Figs 1 2) Of the 6 rats that were not subject to embolization tumour growth could be demonstrated in 3 at repeat angiography 4 to 6 days following the primary examination (Fig 3)

In one of the 2 unpaired rats a decrease in tumour size could be demonstrated at repeat angiography following embolization and reembolization (Fig 4)

At autopsy the livers of both embolized and non-embolized rats were seeded with tumour nodules of different sizes Although the tumour nodules seemed somewhat smaller in embolized animals the difference was not significant However the larger tumour nodules were more extensively necrotic with a pale dry cut surface in

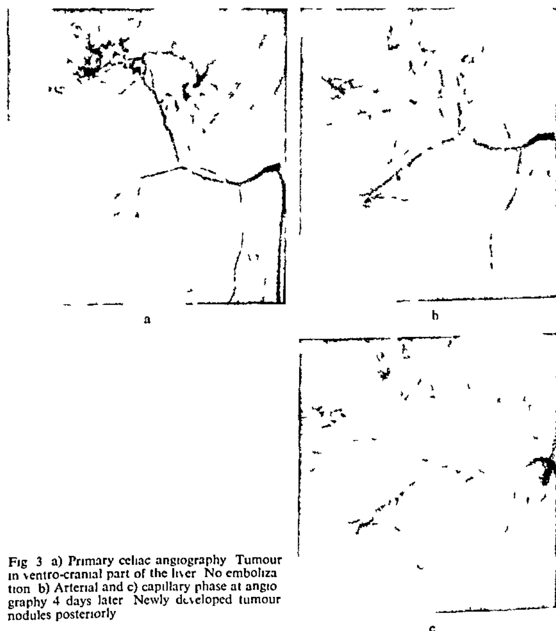


Fig 3 a) Primary celiac angiography Tumour in ventro-cranial part of the liver No emboliza tion b) Arterial and c) capillary phase at angio graphy 4 days later Newly developed tumour nodules posteriorly

Results

The distribution of the findings in the 12 pairs of rats appears in the Table At the primary celiac angiography neoplasms could be demonstrated in 8 of the 12 rats included in the comparison The angiographic appearance of these tumours was the same as described previously (EKELUND et coll 1977) e g the center of the tumour nodules often appeared hypovascular with a hypervascularized rim Partial re canalization of the hepatic artery following embolization with Spongostan occurred in 2 rats after 2 days and reembolization was performed in these animals Partial recanalization was found in 2 further cases after six days

embolized animals Furthermore the intervening liver tissue appeared paler more ischemic in embolized rats

Microscopy confirmed considerably more extensive necroses in embolized tumour nodules than in non-embolized controls These necroses were mainly confined to the larger tumour nodules and were sometimes almost complete while in others a narrow peripheral rim of vital tumour tissue remained (Fig 5) In controls only smaller central parts of some large tumour nodules were necrotic while others had a vital appearance (Fi 6) The smaller tumour nodules appeared mostly vital in both groups of animals

Besides the tumour necroses the liver tissue in 6 of 8 embolized rats was necrotic in fairly large regions (Fig 7) leaving small islands of vital tissue mainly located around portal tracts The necroses often were localized in the vicinity of tumour nodules Such liver necroses were not observed in non-embolized rats with the exception of minor lesions in one animal

Discussion

Primary as well as secondary malignant hepatic tumours receive their main blood supply from the hepatic artery (BREEDIS & YOUNG 1954) It has been shown in man as well as in experimental animals that ligation of the hepatic artery result in tumour necrosis (NILSSON & ZETTERGREN 1967 ALMERSJÖ et coll 1972) Hepatic dearterializa tion is however promptly followed by resupply of the liver through development of collateral circulation (BENGMARK & ROSENGREN 1970 WIRTANEN & KAUDE 1973) An experimental technique for transcatheter embolization of hepatic tumours in the rat was developed by EKELUND et coll (1977) demonstrating that embolic occlusion of the hepatic artery with peripheral extension apparently resulted in less collaterals It was also evident that the arterial supply to these experimental tumours could be temporarily arrested resulting in tumour necrosis as demonstrated at microscopy As spontaneous tumour necrosis also occurs the present comparison was under taken A significant difference in the degree of tumour necrosis was found between embolized and non embolized animal (Table) Necroses in larger embolized tumours were far more extensive although spontaneous necroses occurred in non embolized controls

One important feature of the embolization is its effect on non tumourous liver tissue Transcatheter Spongostan embolization of normal rat livers has previously been reported to cau e no obvious ischemic injury to the parenchyma while an apparently greater ensitivity to anoxic injury of intervening liver tissue in tumour infiltrated livers was found (EKELUND et coll 1977) In the present series the same results i e necrosis of liver tissue was microscopically evident in the embolized rats while usually no morphologic injury was found in non-embolized rats In this context the report of CHO et coll (1976) on the effect of experimental hepatic artery



Fig 5

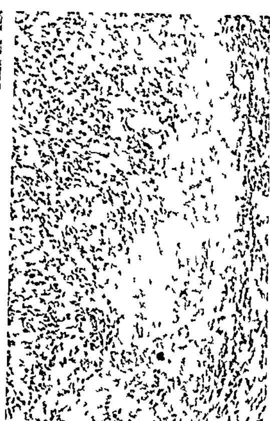


Fig 6



Fig 7

Fig 5 Extensive necrosis in tumour nodule (upper half) in embolized rat leaving only a narrow rim of vital tumour tissue in the periphery Extensive necrosis in adjacent liver tissue (lower half) with small preserved islands of vital tissue around portal tracts (→) Hematoxylin-erythrosin ×40

Fig 6 Vital tumour tissue (left) in nonembolized rat Hematoxylin-erythrosin ×40

Fig 7 Liver necrosis in embolized rat with leukocyte reaction along necrotic liver trabeculae Small island of preserved tissue in upper right corner Hematoxylin erythrosin ×55

von Ratten ohne embolisierte Lebertumoren verglichen Eine partielle Rekanalisation der Arteria hepatica wurde bereits 2 bis 6 Tage nach der Embolisierung nachgewiesen Es wurde eine verminderte Vaskularisation der Tumoren nach der Embolisierung nachgewiesen und bei einigen der Tiere auch eine Abnahme in der Tumorgrosse Die Mikroskopie zeigte ein signifikant hoheres Ausmass von Tumornekrose bei embolisierten Tumoren von grosser Grosse Eine Nekrose von normalem Lebergewebe wurde im verschiedenen Umfang bei embolisierten Ratten gefunden wahrend keine ischamische Schadigung in den Lebern der meisten der nicht embolisierten Tiere zu finden war

RESUME

Apres embolisation artérielle par cathéter au moyen de Spongostan (99 3 ° de gelatine analogue au gelfoam) sur un groupe de rats ayant des tumeurs hepatiques expérimentales les signes angiographiques et microscopiques ont été comparés avec ceux d un groupe de rats ayant des tumeurs hepatiques non embolisées Une recanalisation partielle de l artère hepatique a été mise en evidence au bout de 2 à 6 jours Une diminution de la vascularisation des tumeurs a pu etre mise en evidence après embolisation et meme sur quelques animaux une diminution de la taille de la tumeur L examen microscopique a révélé une étendue significativement plus grande de la necrose tumorale dans les tumeurs embolisees de gros volume Sur les rats embolises on a trouve à un degré variable une necrose de tissus hépatique normal alors qu il n y avait pas de lésion ischémique évidente dans le foie de la plupart des animaux non embolisés

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embolization on liver function in normal dogs is of interest. They demonstrated a temporary decrease in liver function as measured by SGPT, alcaline phosphatase BSP test and bilirubin, followed by recovery within 6 weeks. The portal circulation (and collaterals) is thus sufficiently effective to prevent serious ischemic injury to the normal liver, but the risk of inducing necrosis of preserved tissue in tumour infiltrated livers should be borne in mind when embolization is considered.

In the previous series (EKELUND et coll. 1977) some initial problems were encountered with abscess formation secondary to embolic occlusion causing animal death. Prophylactic antibiotic treatment controlled this situation: the same regimen might also be of value in the clinical management of patients.

Experimental investigations of transcatheter embolization have been concerned with the control of various bleeding sites (CHUANG & REUTER 1975, CHUANG et coll. 1975) and with the comparison of the effect of various embolic materials (BARTH et coll. 1977). The latter authors found autologous clot, oxycel and gelfoam in domestic swine to have a temporary occlusive effect. This is in good agreement with the present results using Spongostan powder (99.3 % gelatin—similar to gelfoam) demonstrating a partial revascularization already after 2 to 6 days. However it should be pointed out that species differences regarding the clotting mechanism exist.

Transcatheter arterial embolization of hepatic neoplasms in man has been reported in a few cases (DOYON et coll., GOLDSTEIN et coll.). However, the clinical application of this technique should be supplemented by experimental investigations. Using the present experimental model, a comparison of the survival rate between a group of animals with embolized hepatic tumours and one with non-embolized tumours should be of great interest and the evaluation of the combined effect of embolization and infusion of cytotoxic agents or immunologic manipulations also seems feasible.

SUMMARY

After transcatheter arterial embolization with Spongostan (99.3 % gelatin—similar to gelfoam) in a group of rats with experimental hepatic tumours, the angiographic and microscopic findings were compared with those in a group of rats with non-embolized liver tumours. Partial recanalization of the hepatic artery was demonstrated already after 2 to 6 days. Reduced vascularization of tumours could be demonstrated after embolization and in a few animals even decrease in tumour size. Microscopy revealed a significantly greater extent of tumour necrosis in embolized tumours of large size. Necrosis of normal liver tissue was found to a varying degree in the embolized rats, while no ischemic injury was evident in livers of most non-embolized animals.

ZUSAMMENFASSUNG

Nach arterieller Embolisierung durch einen Katheter mit Spongostan (99.3 % Gelatine, ähnliches Gelfoam) bei einer Gruppe von Ratten mit experimentellen Lebertumoren wurden die angiographischen und mikroskopischen Befunde mit solchen bei einer Gruppe

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TRANSCATHETER ARTERIAL EMBOLISATION IN NASOPHARYNGEAL ANGIOFIBROMA

P KATSIOTIS G TZORTZIS and CH KARAMINIS

Transcatheter arterial embolisation was first introduced in the treatment of spinal cord angioma and arteriovenous fistula (NEWTON & ADAMS 1968 DOPPMAN et coll 1971 DJINDJIAN 1974 1975) It was later used in similar lesions and vascular tumors in other regions either as a curative method or preoperatively in order to control and limit profuse bleeding during surgery DJINDJIAN (1975) suggested its use in the treatment of juvenile nasopharyngeal angiofibroma which is an infrequent benign fibrous highly vascular tumor occurring in males before or shortly after puberty

Material and Methods

During the past 18 months 4 males between 12 and 19 years of age were admitted to this hospital with obstructive upper respiratory tract symptoms and signs and episodes of epistaxis In 2 of them biopsy was followed by profuse bleeding which was eventually controlled in both cases microscopy suggested nasopharyngeal angiofibroma

At radiography of the skull including views of the nasopharynx the basal projection was found to be the most informative The conventional radiography was supplemented with tomography in 2 of the cases Bilateral selective internal and external carotid angiography was performed in all 4 patients in order to demonstrate the extent of the tumor and the feeding vessels (Fig 1 a b)

This article is based on a report presented at the XIVth International Congress of Radiology Rio de Janeiro 1977 Submitted for publication 17 February 1978

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The femoral route was employed since it allows the whole angiographic procedure to be completed in one session with less discomfort for the patient and less exposure for the operator Subtraction and magnification films in lateral projection during arterial and capillary phases were found to be specially valuable for the detailed demonstration of the tumor (Fig 1 a b)

On completion of the angiography the tip of the catheter was in 3 cases manipulated into the feeding arteries which in all 4 cases were the internal maxillary artery and the ascending pharyngeal artery The exact position of the catheter was controlled by a test injection of 2 to 3 ml of contrast medium In the fourth case the embolisation procedure was performed in a separate session

Ten to 12 strips of gelfoam each 1 mm thick and about 1/2 cm long were then soaked into a syringe filled with saline and injected through the catheter into the maxillary artery This was repeated two to three times After each gelfoam injection the proper position of the tip of the catheter was controlled by a test injection of contrast medium and in order to see whether reflux of the injected medium occurred

On completion of the embolisation 5 ml of contrast medium was injected and a series of lateral films was exposed during 12 seconds in order to evaluate the immediate result This apparently long period was found to be necessary since the flow in the catheterized artery was heavily impaired after embolisation (Fig 1 c d)

The patients were kept under close clinical observation for at least three days after th procedure Subfebrile temperature and pain in the region of the masseter with trismus on the side of the embolized internal maxillary artery occurred in 3 patients All these symptoms and signs subsided within a week after proper medication One patient complained of numbness and pain in the region of the ear and mastoid which correlated well with an obstruction of the posterior auricular artery The first patient developed a right hemiparesis with dysphasia immediately after the procedure In this case the post-embolisation angiography revealed a reflux of the contrast medium into the internal carotid artery The patient s condition improved slowly and six months later he had completely recovered

Following the embolisation rhinoscopy showed ischemia in the region of the tumor which was definitely reduced in size The patients were operated upon within two weeks after the embolisation The blood loss during the surgical removal of the tumor was remarkably small in contrast to that in patients who were operated upon after stilboestrol therapy On examination of the excised tumor evident ischemic necrotic foci and vascular thrombosis were found

Discussion

Juvenile angiofibroma is a benign but highly vascular fibrous tumor with a characteristic angiographic appearance This makes it possible to avoid biopsy which may be dangerous

The tumor acts in some respects as an arteriovenous malformation Radiation

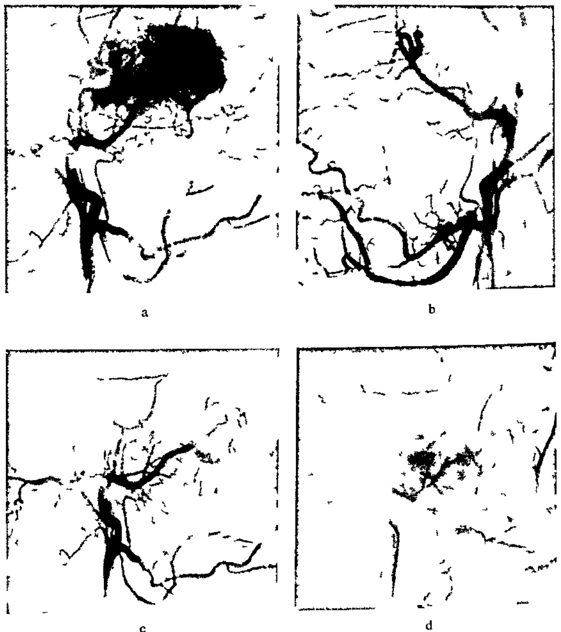


Fig 1 Case 4 Boy 12 years old a) Selective left external carotid angiography Subtraction Vascular network delineating the tumor Feeding vessels mainly from the dilated internal maxillary artery but also from the ascending pharyngeal artery Tumor extending into spheno palatine region b) Selective right external carotid angiography Small pathologic vascularity in the roof of the naso pharynx projected above the middle part of the trunk of the internal maxillary artery c) Angiography after embolisation of the left internal maxillary artery Internal maxillary artery cut off distally as well as the ascending pharyngeal artery There is also cutting off of many branches of the internal maxillary artery Some back flow towards the trunk of the external carotid artery d) Postembolisation angiography late phase Stagnation of the contrast medium in the internal maxillary artery Tumor vascularity reduced Tip of the catheter high up in the origin of the internal maxillary artery

carotid artery and the cerebral vessels This may easily happen in cases where the carotid bifurcation is located high in the neck (DJINDJIAN) as was the case with the first patient in the present series In order to prevent such accidents superselective catheterization of the feeding vessels should be tried and a test injection should be performed after each embolus injection Balloon tip catheters can in some cases be useful The use of vasoconstrictive drugs injected through the catheter after embolisation could possibly help in preventing reflux

The procedure is well tolerated and has the advantage that it can be repeated where surgery is exceedingly hazardous in cases already subjected to surgical failure After embolisation total excision of the tumor is rendered possible with only insignificant blood loss It constitutes an indispensable preoperative procedure for the successful cure of juvenile angiofibroma

SUMMARY

Transcatheter arterial embolisation using gelfoam particles has been used in 4 young male patients with nasopharyngeal angiofibroma The procedure proved to be extremely useful preoperatively in controlling and limiting profuse bleeding during surgery allowing total excision of the tumor

ZUSAMMENFASSUNG

Eine arterielle Embolisierung uber einen Katheter unter Verwendung von Gelatine Partikeln wurde bei 4 jungen Patienten mit nasopharyngealen Angiofibromen vorgenommen Das Verfahren erwies sich als ausserordentlich brauchbar zur praoperativen Kontrolle und Begrenzung von profusen Blutungen wahrend der Operation wodurch eine totale Exzision des Tumors moglich wurde

RESUME

L embolisation arterielle par catheterisme utilisant des particules de gelfoam a ete utilisée chez 4 jeunes hommes atteints d angio fibrome nasopharyngien Cette technique s est montree tres utile en pre operatoire pour maitriser et limiter les hemorragies profuses pendant l operation permettant ainsi une excision totale de la tumeur

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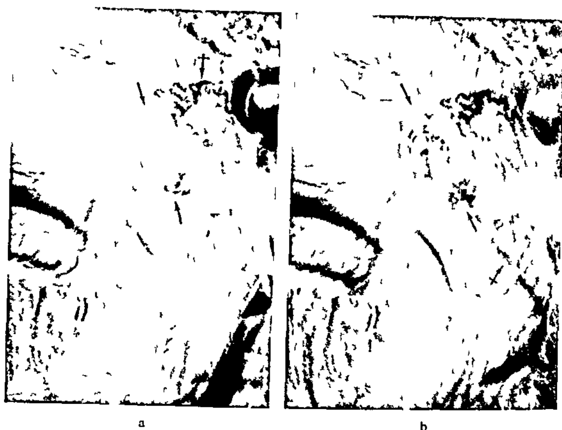


Fig 2 a) Left common carotid angiography Previous ligature of the external carotid artery at a level below the origin of the internal maxillary artery Tumor (→) fed by dilated sphenoidal branches of the internal carotid artery (↔) b) Late phase Internal maxillary artery filled through a collateral anastomotic channel (+→) feeding the tumor (→)

therapy has been tried but proved unsuccessful Stilboestrol therapy is said to limit and diminish the vascularity of the tumor (SCHIFF 1959 WALIKE & MACKAY 1970) Surgical ligature of the feeding vessel or of the external carotid artery and partial excision of the tumor is followed by recurrence (BILLER et coll 1974) Collaterals develop either from the internal carotid artery through its sphenoidal branches or from the external carotid artery (Fig 2) Anastomoses between muscular branches of the vertebral artery on the side of the tumor or from the contralateral external carotid artery have also been reported (WILSON & HANAFEE 1969)

The external carotid branches feeding the tumor can be occluded by transcatheter arterial embolisation thus reducing its vascularity However it cannot be applied to feeding vessels from the internal carotid artery which sometimes occur particularly in extensive tumors

The difference between surgical ligature of feeding vessels and transcatheter arterial embolisation is that the injected emboli follow the blood flow and lodge in distal small arterial branches The position of the catheter and the flow must be carefully observed during the procedure to ensure that emboli do not pass into the internal

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BLOOD INFLOW INTO VASCULAR CATHETERS FOLLOWING INJECTION OF SALINE SOLUTION AND CONTRAST MEDIUM

Model experiments

MATS DAHLBORN and ULLA SÖDERLUND

Thromboembolism following introduction of catheters into arteries is a well known complication of the procedure Thrombocytes aggregate on the vessel wall or on the outer surface of the catheter and are followed by formation of fibrin sleeves (JACOBSSON & SCHLOSSMAN 1969) When blood enters the catheter lumen the same mechanism also applies for the inner surface of the catheter (SCHLOSSMAN 1973) Intermittent flushing of intravasal catheters with saline solution or with contrast medium is the usual means to avoid this event According to HAWKINS & HERBERT (1974) contrast medium should be more effective in preventing blood clot formation than saline solution DAHLBORN et coll (1978) have shown that the effect of contrast medium is gravity dependent in that the medium leaks out more rapidly from a catheter when the tip is directed downwards than upwards As the mechanism of blood inflow into catheters following injection of saline solution has not previously been analysed catheters were flushed with saline solution and water soluble contrast media using an experimental model The results are now reported

Methods

A blood circulation model was used consisting of an electric motor pump connected to plastic tubes filled with blood from human donors (900 ml blood + 130 ml ACD-solution formula A US pharmacopeia) The pump was generating pulsative

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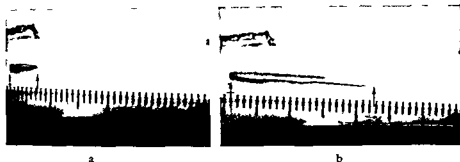
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a b

Fig. 2. Translucent tube with a catheter glued to its interior surface. Blood inflow into the catheter one min after fluid injection and catheter tap closure. Blood located a) above Isopaque Cerebral b) below isotonic saline solution. Length of blood column (→). Catheter tip (+→)

Table 1

Number of experiments following a single fluid injection

	Tip of catheter directed				Total
	Upwards		Downwards		
	Up-stream	Down stream	Up-stream	Down stream	
Isopaque Cerebral	3	4	3	4	
Ar paque	0	4	0	4	
Isotonic saline solution	3	4	3	4	
Hypertonic saline solution	0	4	0	4	
Total	6	16	6	16	44

Table 2

Number of experiments with continuous fluid injection

	Tip of catheter directed				Total
	Upwards		Downwards		
	Up-stream	Down stream	Up-stream	Down stream	
Isopaque Cerebral	8	8	8	8	
Isotonic saline solution	8	8	8	9	
Total	16	16	16	17	65

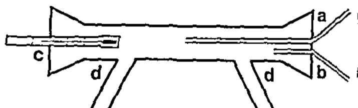


Fig 1 Translucent tube with transparent catheter for blood inflow recording (a) catheter for blood pressure recording (b) and thermometer (c) The tube was connected to a pump (d)

movements of the blood imitating the effect of the heart beats The plunger move ments and the volume per beat were adjustable within certain limits The pulse rate was constant during each experiment and varied between 32 and 44 beats/min A translucent tube of plastic material (ID 10 mm) was connected horizontally to the circulation system (Fig 1) On the interior surface of the tube a transparent poly ethylene catheter (ID 1 15 mm) was glued The free surface of the catheter was painted white to give a suitable background to the blood inflow into the catheter when looking through the translucent tube wall A catheter for blood pressure recording and a probe for electromagnetic blood flow registration were connected to the tube The blood pressure varied between 160/0 and 240/30 mmHg the blood flow between 380 and 700 ml/min Both factors were kept constant during each experiment To avoid alterations in density and viscosity of the fluids during the experiments a water thermostat kept the temperature of the system on a physiologic level

In all the experiments the blood inflow into the catheters was documented photo graphically on slides (Fujichrome R 100) In 44 of the total 113 experiments the blood flow into the catheter was recorded after a single fluid injection into the catheter (Table 1) During each experiment 9 films were exposed 0 15 and 30 s and 1 1 5, 2 3 4 and 5 min following the catheter tip closure at the end of the injection The length of the blood inflow into the catheter was measured on the films In the re maining 65 experiments continuous fluid injections into the catheter were performed with an automatic syringe pump with adjustable injection speed (Table 2) The following speeds were used 0 5 1 2 2 6 and 4 ml fluid/s During these injections the pulsative blood inflow was recorded photographically by single films and esti mated by eye and its maximum and minimum length noted During the experiments the catheter tip was directed either 5° upwards or 5° downwards upstream or down stream The following fluids and densities at 20 to 25 C were used Isopaque Cerebral (meglumine/calcium metrizoate 280 mg I/ml 1 31 g/ml) Amipaque (metrizamide 2 [3 acetamido 5 N methylacetamido 2 4 6 triiodobenzamido] 2 deoxy D glucose 1 057 g/ml) isotonic (1 004 g/ml) and hypertonic saline (1 055 g/ml) solutions The Amipaque and the hypertonic saline solutions were given densities close to the density of ACD blood (1 056)

Results

In all experiments with a single injection of the flush fluid the lumen of the catheter was completely filled with the fluid at the end of the injection A few seconds later

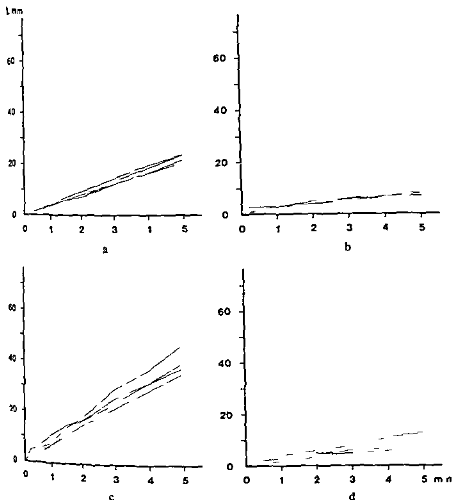


Fig 4 Blood inflow into the catheter after injections of Amipaque with a) catheter tip directed upwards, b) downwards and of hypertonic saline solution with c) tip directed upwards d) downwards. L length of inflow

was directed downwards than when directed upwards (Fig 3 c d) The average length of the blood inflow 60 s after the injection was 9 mm and 17 mm respectively and the corresponding figures after 5 min were 19 mm and 59 mm No differences were found in the amount and speed of the blood inflow when the catheters were directed downstream or upstream

In the experiments with Amipaque the blood inflow into the catheter was much less than in those with Isopaque Cerebral when the tip was directed downwards (Figs 3 b 4 b) However when the tip was directed upwards no difference between the contrast media (Figs 3 a 4 a) was recorded When hypertonic saline solution

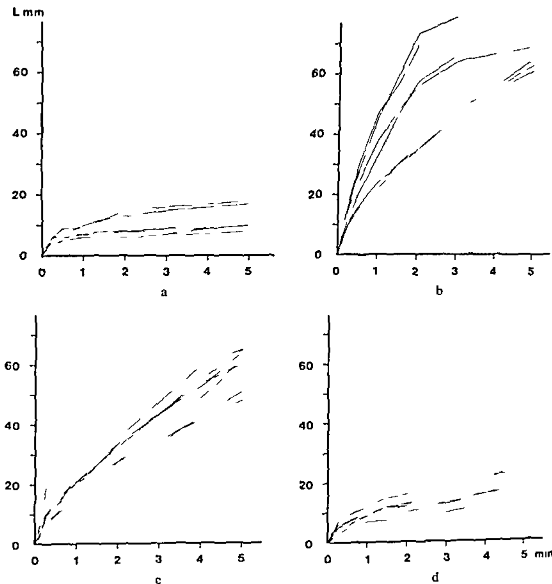


Fig 3 Blood inflow into the catheter after injections of Isopaque Cerebral with a) catheter tip directed upwards b) downwards and of isotonic saline solution with c) tip directed upwards d) downwards L = length of inflow

the flush fluid in the catheter tip invariably became partially replaced by blood forming a layer below the isotonic and hypertonic saline solutions and the Amipaque and above the Isopaque Cerebral (Fig 2) The inflow of blood increased continuously during the 5 min of observation In the experiments with Isopaque Cerebral the length of the blood inflow was less when the catheter tip was directed upwards than when directed downwards (Fig 3 a b) The average length of the blood inflow 60 s after the end of injection was 7 mm and 33 mm respectively The corresponding figures after 5 min were 12 mm and 66 mm When isotonic saline solution was used as flush fluid the blood inflow into the catheter tip was less when the catheter tip

essure and the blood flow varied within an almost physiologic range in all experiments and could only have minor influence on the rate of blood inflow regardless of the flush fluids used Furthermore the catheter tip was placed in a fixed position peripherally in the tube while the tip of an intraarterial catheter oscillates and may be located anywhere in the lumen of the artery The blood flow in an artery is known to differ considerably in the central and peripheral parts of its lumen This phenomenon might at least theoretically have some influence on the blood flow into the catheter However as the positioning of the tip of the catheter upstream or downstream did not have any effect on the blood inflow the influence of the tip whether located centrally or peripherally in the tube should be of minor importance The present results using Isopaque Cerebral coincide closely with those previously achieved in vivo (DAHLBORN et coll) indicating that the circulation model experiments generally are relevant for the corresponding intraarterial conditions

The blood inflow into the catheter tip was quite different with Isopaque Cerebral and isotonic saline solutions as flush fluid Isopaque Cerebral was replaced by blood situated above the contrast medium and leaked out more rapidly when the catheter tip was directed downwards The opposite results were achieved with isotonic saline solution the blood was situated below the flush fluid leaking out of the catheter faster when the tip was directed upwards These differences must be due to different densities of the fluids the ACD blood has lower density than Isopaque Cerebral and higher than isotonic saline solution The influence of the density of a flush fluid on the blood inflow into a catheter was established when a contrast medium and a saline solution with a density close to that of blood were compared with the other solutions However the results also indicated that other factors than the density such as the viscosity might be of significance because different effects on the inflow of blood were evident when using Amipaque or saline solution of densities almost identical to that of blood

The pulsative movements of the blood inside the catheter during continuous fluid injection were larger with isotonic saline solution than with Isopaque Cerebral and both fluids required a rather high flow rate to keep the catheter free of blood Thus continuous injection did not seem to have any advantages over repeated single injections followed by closure of the catheter tip particularly when isotonic saline solution was used Neither Isopaque Cerebral nor isotonic saline solution is a satisfactory flush fluid An ideal solution for this purpose should have other physical properties better corresponding to those of the blood

SUMMARY

Using an experimental model of the arterial system inflow of blood into polyethylene catheters following injection of two contrast media isotonic and hypertonic saline solutions was investigated The experiments included an analysis of the influence of the density of the solutions and the orientation of the catheter as well as the effect of single fluid injection and continuous flushing of the catheter

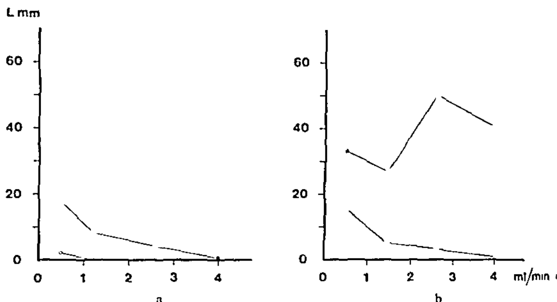


Fig 5 Blood inflow into the catheter during continuous fluid injection with a) Isopaque Cerebral and b) isotonic saline solution The upper curves (●—●) represent mean blood inflow during systole and the lower curves (○—○) during diastole

was used the blood inflow was slightly less than with isotonic saline solution This difference was recorded with the catheter tip directed upwards as well as downwards (Figs 3 c d 4 c d)

When the injector was used an equilibrium of blood inflow was established within a few seconds following the opening of the tap to the syringe The plunger movements of the pump caused synchronous pulsative movements of the blood in the catheter tip These pulsative movements were generally larger using isotonic saline solution as flush fluid than Isopaque Cerebral The blood inflow decreased with increasing flow velocity Using Isopaque Cerebral a flow velocity of 1 2 ml/min kept the catheter free of blood in diastole and at a flow velocity of 4 ml/min no blood passed into the catheter tip (Fig 5 a) However when isotonic saline solution was used there was still a large blood inflow in systole at a flow velocity of 4 ml/min (Fig 5 b)

Discussion

A circulation model was used to analyse the differences of blood inflow into vascular catheters using contrast medium and saline solution as catheter flush fluids The circulation model made it possible to observe the blood flow into the catheter tip directly by eye through the translucent plastic tube and the catheter It is true that the artificial system with a mechanical pump and plastic tubes with stiff walls will generate steeper plunger movements and higher pressure amplitudes than in a human artery under in vivo conditions The large pulsative movements of the blood in the catheter tip during continuous fluid injection could be due to disparities in mechanical properties of the model and the biologic system However the blood

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TENDINOGRAPHY FOR DIAGNOSING INJURIES TO TENDONS AND LIGAMENTS

S GREVSTEN and K ERIKSSON

Injuries resulting in partial rupture of a tendon or rupture of a ligament for example the cruciate ligament are sometimes difficult to evaluate clinically (RIEDE 1966 LILJEDAHL et coll 1966 LJUNGQVIST 1968)

The methods available today for examining tendon injury are radiography of the soft tissue (KAGER 1939) of the tendon sheath (ARNER & LINDHOLM 1959 ARNER et coll 1958/1959 1960) of the bony attachment and arthrography and electromyography (PERSSON & LJUNGQVIST 1971) These methods are indirect and accordingly the diagnostic precision is sometimes inadequate

A radiographic method with direct injection of contrast medium into tendons or ligaments is now presented It was worked out on an autopsy material and tested in experimental animals and two healthy subjects The optimum amount and concentration of the medium were sought and the reaction of the tendon to the injection assessed The use of the method is illustrated in two traumatic clinical cases

Anatomy

A tendon consists of collagenous fibres arranged in bundles and surrounded by connective tissue (internal peritendineum) containing small blood vessels (STUCKE 1949) The fibres of the tendon anastomose to one another and are presumably as long as the tendon itself (BUCHER 1962 SCHATZKER & BRANEMARK 1969) Between

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ZUSAMMENFASSUNG

Unter Verwendung eines experimentellen Modells des arteriellen Systems wurde der Einstrom von Blut in Polyäthylenkathetern im Anschluss an eine Injektion von zwei Kontrastmitteln isotonischen und hypertonischen Salzlosungen untersucht Die Experimente umfassten eine Analyse des Einflusses der Densität der Losungen und der Richtung des Katheters sowie des Effektes einer einzelnen Injektion und der einer kontinuierlichen Spulung des Katheters

RÉSUME

En utilisant un modèle expérimental du système artériel les auteurs ont étudié l entrée de sang dans les cathéters en polyéthylène après injection de deux moyens de contraste et de solution salée isotonique et hypertonique Ces expériences comprenaient une analyse de l influence de la densité des solutions et de l orientation du cathéter ainsi que de l effet d une injection unique de liquide et d une injection continue dans le cathéter

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Fig 1 a) 4 ml injected into the Achilles tendon Entire tendon filled and evident fibrous structure b) 6 ml injected into the same tendon, slightly more diffuse filling but *still* intact synovial margin c) 8 ml injected *rounded defects* at the synovial margin d) Leakage after injection of 10 ml

Table 2

Amount (ml) of contrast medium infusible into cruciate ligam nts

Age	Sex	Minimum amount filling the entire ligament		Amount producing diffuse leakage	
		Anterior	Posterior	Anterior	Posterior
57	M	2	2	9	10
17	M	—	—	8	9
?9	M	1	2	8	7
53	M	1	1 5	9	9 5

Material and Method

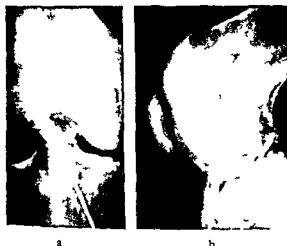
Autopsy material Twelve Achilles tendons and 8 cruciate ligaments in individuals with no history of pathologic conditions of the lower extremities were injected with Uro rafin 45° diluted with isotonic saline to concentrations of *30 20 or 15 per cent*

Table 1

Amount (ml) of contrast medium infusible into Achilles tendon in 6 autopsy cases

Age Sex	Minimum amount filling the entire tendon	Amount producing defect at the tendon margin	Amount producing diffuse leakage
53 M			
Right	4	8	10
Left	4	7	9
84 M			
Right	—	—	11
Left	—	—	11
62 F			
Right	—	—	9
Left	—	—	9
29 M			
Right	4	8	11
Left	5	9	10
57 M			
Right	4	6	7
Left	3	7	8
17 M			
Right	5	8	10
Left	5	7	9

the collagenous fibres fibrocytes are arranged in rows The internal peritendineum communicates with the outer layer of connective tissue the external peritendineum outside which a thin mobile layer exists Tendons and ligaments intended for less extreme forces are attached to the fibrous layer of the periosteum This fibrous layer consists of a network of collagenous and elastic fibres Tendons and ligaments intended for extreme forces are anchored in apophyseal bone tissue Such is the case at the lateral and medial internal tubercules on the tibial condyle (the anterior and posterior cruciate ligaments) at the tibial tuberosity (the patellar tendon) and the calcaneal tubercle (the Achilles tendon) Here the fibres are anchored with the fibres radiating into the bone in the fashion of a brush pressing against a flat surface (MOLLIER 1937 SCHNEIDER 1956 ALTMAN 1963) The tendon fibres are attached to the compact bone through the fibrous layer and the cambium When a tendon runs a longer distance it is covered by a tendon sheath This sheath (the vagina tendinis) has the same structure as a joint capsule It consists of a fibrous membrane which in some instances is strenghtened by an additional network of connective fibres Its inner surface is lined by a synovial membrane carrying blood vessels and nerve fibres



a b

Fig 3 Injection into the anterior ligament Route of administration through the spongy bone of the tibial condyle

After 12 to 15 days all rabbits were killed A specimen consisting of the entire Achilles tendon with its bone attachment and muscle insertion was taken All tendons were examined microscopically after decalcification and staining with van Gieson

Human experiments In 2 healthy subjects (the authors) both Achilles tendons were examined either once or twice The amount of contrast medium used varied between 2 and 4 ml and the concentration between 15 and 30 per cent No local anaesthetic was used The injection rate was about 3 ml/min One cruciate ligament was also examined in both subjects In one subject 2 ml and in the other 3 5 ml of Urografin was injected The contrast medium was diluted with a local anaesthetic to a concentration of 20 per cent This examination was performed through a minor incision medial to the tibial tuberosity but otherwise as described in the autopsy material The purpose of these examinations was to estimate if any examination difficulties or drawbacks existed and to determine the appropriate concentration of Urografin

The method was also applied in a patient with injury to an Achilles tendon in which a calcification had developed A further illustration is given intraoperatively in a patient with a suggested rupture of the anterior cruciate ligament

Results

Autopsy material The amount of contrast medium infusible into an Achilles tendon and a cruciate ligament differed (Tables 1 2) but the distribution of the medium was similar After one to 2 ml only a small part of the tendon contained contrast medium The fibrous structure was clearly visible When another one to 2 ml were added

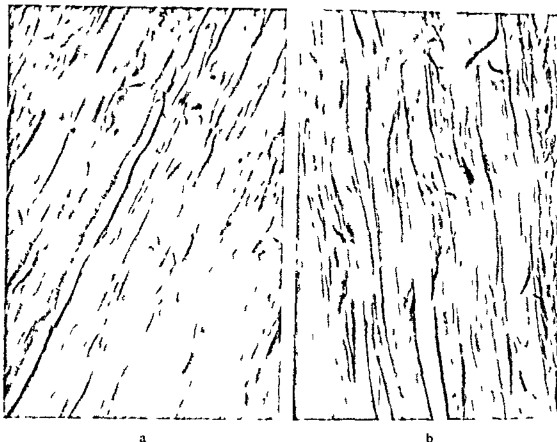


Fig 2 Light microscopy of rabbit Achilles tendons a) Injected with 2 ml of Urografin 20 12 days previously b) Control No pathologic reaction Van Gieson × 1 000

For examination of the Achilles tendon the foot was held in 15 to 20 dorsiflexion A cannula was inserted in proximal direction into one third of the tendon via its apophyseal bone attachment Contrast medium was then injected through the cannula into the tendon and films were exposed after each ml injected

The examination of the anterior cruciate ligament was performed by injection through a cannula (Venflon) introduced into a channel from the tibial tuberosity to the anterior tibial tubercle obtained with an awl through the spongy bone under fluoroscopy

Animal experiments The reactions of the tendon tissue to the injection were evaluated on rabbits In 12 rabbits contrast medium was injected into the left Achilles tendon 9 rabbits were used as controls (All rabbits had their right leg immobilized in plaster for another investigation which did not interfere with this one)

Under fluoroscopy the rabbits were injected with 2 ml of Urografin 20 % the needle was inserted into the tendon through its bone attachment Films were exposed immediately after the injection

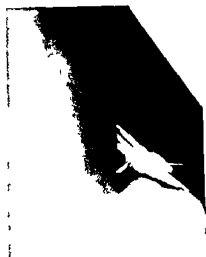


Fig 5 Direct puncture of the Achilles tendon with injection of medium Leakage where the tendon is penetrated

bined with a feeling of muscle cramp lasting a few minutes Thereafter no discomfort at all was exp rienced One of the subjects played a squash match without any discomfort about one hour after injection of 4 ml of contrast medium into his Achilles tendon (no local anaesthetic)

The contrast medium disappeared relatively rapidly from the tendon the films had to be exposed within 5 min After 10 to 15 min the medium was quite diffuse although a concentration of 30 per cent was used At least this concentration is recommended when Urografin is used as contrast medium for tendinography

In the examination of the 2 healthy cruciate ligaments no discomfort was felt during the injection When the effect of the local anaesthetic had disappeared one of the subjects had almost no discomfort (2 ml injected) The other had a boring pain for 3 to 4 hours (3 5 ml injected) For demonstration of the cruciate ligaments 2 to 2 5 ml of contrast medium appear to be sufficient It was evident that Urografin 20 was too low a concentration at least 30 per cent is needed (Fig 3)

Traumatic case A case with a partially ruptured and calcified Achilles tendon was examined

On comparison of the preoperative films and films exposed during operation it was evident that the contrast medium passed from the distal part of the tendon through the remaining not injured fibres into the proximal part of the tendon defining the tendon defect (Fig 4)

Discussion

Contrast medium can be injected into a tendon or ligament in different ways A cannula can be inserted perpendicular to the tendon in its middle part This route of



Fig 4 Achilles tendon partially ruptured through a calcified part Contrast medium injected runs along the remaining fibres a) Conventional film b) Tendinography c) Photograph taken at operation (calcification →)

the whole tendon was infused and the fibrous structure could still be observed (Fig 1 a) Addition of a further one to 2 ml (totally 5–6 ml) caused no significant changes but in some cases the contrast was slightly more diffuse centrally and the fibrous structure was no longer quite evident (Fig 1 b) A tendon containing 7 to 8 ml of contrast medium usually displayed small defects at its margin and centrally the medium was quite diffuse (Fig 1 c) Leakage of contrast medium from the tendon in all directions usually occurred at 9 to 10 ml (Fig 1 d) The amount of contrast medium injected when leakage occurred ranged from 7 to 11 ml in the 12 tendons observed (Table 1)

Animal experiments No pathologic reaction was observed in any of the 12 rabbits injected (Fig 2), the appearances being similar in these 12 rabbits and the 9 controls

Human experiments The examination of the Achilles tendon in the 2 healthy subjects gave very little discomfort even though no local anaesthetic was used On injection of the contrast medium into the tendon a tense feeling but no real pain was felt The sensation could be described as a firm grip around the tendon region com

Between the bony insertion and the muscle junction a tendon may be tortuous or display interdigitation to varying extents (CUMMINS et coll 1946 KELLER 1951 BIRO & TARSOLY 1967 BARFRED 1973) the less the tortuosity the more the interdigitation In cases with marked interdigitation even a suitable amount of contrast medium filling the entire tendon may give a diffuse image Too much medium gives all types of fibrous structures the same appearance The minimum amount of medium needed to infuse the entire Achilles tendon appeared to be 3 to 4 m (Table 1) However a 10 cm long circular tendon with an average diameter of one to 1 5 cm has a calculated total volume of between 7 5 and 15 ml Moreover the length of a tendon is extremely variable between 5 and 15 cm Thus it seems reasonable to assume that the amount of contrast medium required might be even more than 4 ml for individuals with larger tendons

No inflammatory reactions were observed at microscopy 12 to 15 days after injection of 2 ml of Urografin 30 % into the Achilles tendon of rabbits Clinical examinations of human Achilles tendons gave very little discomfort although up to 4 ml of Urografin 30 % were injected into one tendon without a local anaesthetic

The injection of 3 5 ml of contrast medium diluted with a local anaesthetic (20) into the anterior cruciate ligament through an awl channel from the tibial tuberosity to the anterior tibial tubercle caused pain lasting 3 to 4 hours after the effect of the local anaesthetic had disappeared This was probably periosteal pain resulting from the penetration of the spongy bone by the awl but it could also have been a late effect of injection of too much contrast medium into the ligament The subject injected with 2 ml had almost no discomfort The amount of contrast medium should be somewhere in the range of 2 to 3 ml and should be adjusted for each individual case Urografin 20 gave films with poor contrast and subsequent intraoperative examinations of patients with medium of 30 to 40 per cent have shown that a concentration of at least 30 per cent is needed for films of good quality A further illustration of the value of this method is given in Fig 6 This tendinography was performed intraoperatively when exploring a knee for suggested rupture of the anterior cruciate ligament The ligament was covered by a fibrotic and thickened synovial membrane as in lipoma arborecens or Hoffa s disease Without tendinography the ligament would have been believed to be ruptured Even explored with great care destruction of the ligament could easily have occurred

Acknowledgement

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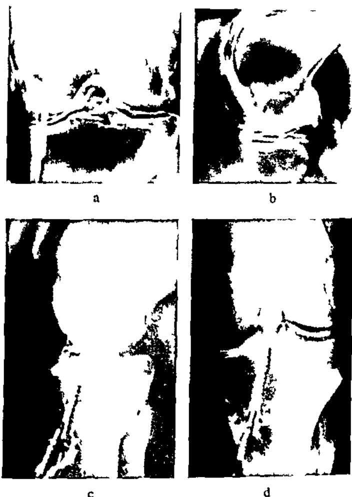


Fig 6 a b) Arhtrography suggests rupture of the anterior cruciate ligament but c d) tendinography demonstrates that the ligament is not injured

injection has clear disadvantages a leakage always occurs at the point of penetration of the tendon (Fig 5) and the contrast medium does not spread satisfactorily in the tendon Almost the same result is encountered following insertion of the cannula into the tendon through the muscle

The best way of introducing the cannula is to force it into the tendon through its bony attachment The tense grip of the fibrous stratum then prevents leakage The cannula must be carefully oriented in the longitudinal direction of the extended tendon In the Achilles tendon this is most easily achieved with the foot in 15 to 20 dorsiflexion The cannula should be inserted subperiosteally through the fibrous stratum at the calcaneal tubercle (ARNER et coll 1958/1959) and advanced to the middle part of the tendon under palpation The anterior cruciate ligament appears to be most easily reached from the medial side of the tibial tuberosity through to bone up to the anterior tubercle (Figs 3 6) The optimum position of the knee is from full extension to 20° flexion

The collagenous fibres of a tendon and certain ligaments such as the cruciate ligaments are as long as the tendon itself (STUCKE BUCHER SCHATZKER & BRÅNEMARK)

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SUMMARY

A radiographic method of tendinography is described In rabbits no inflammatory reaction in the Achilles tendon was observed 12 to 15 days after injection of contrast medium Effects of examination of two healthy subjects and a patient with a traumatic condition are described Suitable amounts and concentrations of contrast medium for examinations of Achilles tendon and cruciate ligaments are discussed

ZUSAMMENFASSUNG

Eine rontgenologische Methode der Tendinographie wird beschrieben Bei Kaninchen wurden keine entzundlichen Reaktionen in der Achillessehne 12 bis 15 Tage nach der Injektion von Kontrastmittel beobachtet Die Wirkungen der Untersuchung bei zwei gesunden Personen und einem Patienten mit einem Trauma werden beschrieben Geeignete Mengen und Konzentrationen von Kontrastmittel zur Untersuchung der Achillessehne und der Kreuzligamente werden diskutiert

RESUME

Les auteurs décrivent une méthode radiographique de tendinographie Ils n ont pas observé de réaction inflammatoire sur le tendon d Achille sur des lapins 10 à 15 jours après l injection de moyen de contraste Ils décrivent les effets de l examen sur 2 sujets sains et un malade atteint de lésions traumatiques Ils discutent les quantités et les concentrations convenables de moyen de contraste pour l examen du tendon d Achille et des ligaments croisés

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Material and Methods

The reference group is identical with the one previously used in Part IV (BERGSTEDT et coll) It comprised 8 patients with mammary carcinoma at an early stage without any sign of paranasal affection metastatic lesion or any other disease of the face or skull

In a series of 25 patients examined by radiography and scintigraphy because of symptoms of paranasal sinus affection 9 patients had a maxillary sinus affection at radio raphy but without purulent secretion on aspiration The clinical diagnosis in thes. patients was allergic rhinitis No patient had a history of purulent nasal infection within ? months

Eleven patients had a maxillary sinus not containing air at radiography and puru lent inflammation on aspiration All had a history of purulent sinuitis In 4 patients the duration of sinuitis was from one to four weeks and in the remaining patients from one month to about one year The duration of symptoms was roughly equally distributed in the two groups

Five of the 25 patients were not possible to classify and were therefore excluded Two of these patients reported purulent secretion which was not confirmed on aspira tion, and in 3 patients only marginal swelling of the sinus mucosa was present

At the first visit a clinical diagnosis was reached in all patients based on history and clinical examination Radiography was then performed and if an affection of the maxillary sinus was confirmed it was supplemented with a facial bone scintigraphy ($^{99}Tc^{m}$DP) This examination included three projections of the paranasal sinuses (BERGSTEDT & LIND 1978) and the scintigrams were classified into 4 groups De finitely normal probably normal probably abnormal and definitely abnormal

The roentgenologic technique included two p a one lateral and one axial projec tion (BERGSTEDT & LIND)

Sinus secretion was obtained by aspiration through a Lichwitz needle inserted through the inferior nasal meatus on the same day or the day after the scintigraphy The secretion was characterized as purulent or non purulent according to CARENFELT & LUNDBERG (1977) When no secretion was obtained 5 ml of sterile saline was in stilled into the antrum and reaspirated to exclude the presence of pus and to obtain a sample for bacteriologic examination (CARENFELT et coll 1978)

Results

The scintigrams were classified as normal with symmetric accumulation of tracer in all patients in the reference group (BERGSTEDT & LIND)

They were con idered as definitely or probably normal in the region of the maxillary sinus affected in all patients with non purulent inflammation (Figs 1 3 Table) and as probably or definitely abnormal (i e the $^{99}Tc^{m}$DP accumulation was abnormally in creased) in all patients with purulent inflammation (Figs 2 3 Table)

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FACIAL BONE SCINTIGRAPHY

V. Differentiation of purulent from non-purulent inflammation of the maxillary sinus

H. E. BERGSTEDT, C. CARENFELT and M. G. LIND

The reaction to bacterial infection or allergy often causes the air of affected sinuses to be substituted by soft tissue or fluid. In patients with a longstanding purulent infection of the maxillary sinus resistant to treatment, or with the possibility of malignant growth, exploratory surgery should be carried out in order to confirm the diagnosis, to eliminate the inflammatory mucosa and to establish a broad communication between the sinus and the nasal cavity for adequate drainage. Non-purulent, possibly allergic inflammatory swelling of the mucosa or a polypoid reaction may cause a radiologic appearance which is identical to purulent sinusitis. In these patients the results of surgical exploration of the sinus do not motivate the operation trauma unless the purpose is to exclude a possible malignant lesion. Some patients have allergic mucosal swelling concomitant with residual purulent infection. It is not possible to differentiate these disorders simply by conventional radiography. In such cases facial bone scintigraphy is more sensitive in demonstrating bone tissue involvement by purulent maxillary sinusitis (BERGSTEDT et coll. 1979). The diagnostic potential of facial bone scintigraphy in differentiating between longstanding purulent and non-purulent inflammation has been evaluated in a small series of patients and the results are now reported.

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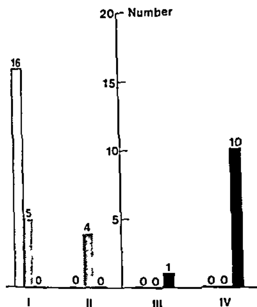


Fig 3 Classification of tracer accumulation in the affected maxillary region I Definitely normal II Probably normal III Probably abnormal IV Definitely abnormal White columns Reference group Grey columns Non purulent Black columns Purulent sinuitis

BERGSTEDT & LIND also indicate that facial bone scintigraphy has a potential clinical value in diagnosing chronic inflammatory involvement of the paranasal sinuses Hypothetically chronic allergic non purulent inflammatory reactions should not influence bone metabolism and ^{99}Tc^{m}DP accumulation in the bone tissue to the same extent as chronic purulent inflammation Osteitic bone reactions are possible to demonstrate at conventional radiography although not in an initial or mild phase and in the thin bone structures surrounding the paranasal sinuses early osteitic reactions are difficult to observe Facial bone scintigraphy has been demonstrated to be more sensitive than radiography in demonstrating bone tissue involvement by purulent maxillary sinuitis (BERGSTEDT et coll)

It was not possible by means of radiography to differentiate between purulent and

Table

Radiography and scintigraphy results I Definitely normal II Probably normal III Probably abnormal IV Definitely abnormal

	Pus	Scintigraphy				Radiography no air in maxillary sinus
		I	II	III	IV	
Reference group 16 sinuses	—	16	0	0	0	0
Non purulent sinuitis 9 sinuses	0	5	4	0	0	9
Purulent sinuitis 11 sinuses	11	0	0	1	10	11

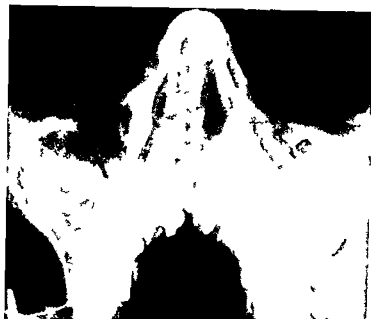



Fig 1 Radiography and scintigraphy in a patient with non purulent sinuitis




Fig 2 Radiography and scintigraphy in a patient with purulent sinuitis

Discussion

The capacity of the bone substance to accumulate intravenously administered $^{99}Tc^{m}DP$ is reported to constitute a sensitive method for demonstrating malignant involvement as well as osteitic reaction of the bone (SILBERSTEIN et coll 1973 TILDEN et coll 1973 DESAULNIERS et coll 1974 GENANT et coll 1974 PAPADIMITRIOU et coll 1974 THRALL et coll 1974 BELLIVEAU & SPENCER 1975 KAYE et coll 1975 LETTS et coll 1975 OSMOND et coll 1975 ROSENTHALL & KAYE 1975 GARCIA et coll 1976 LIND & NATHANSON 1977, BERGSTEDT & HAVERLING 1978) Results reported by

ZUSAMMENFASSUNG

In einer Serie von 25 Patienten hatten 20 einen Sinus maxillaris ohne Luft bei der Rontgen untersuchung in 11 Fallen als Folge einer purulenten und in 9 einer nicht purulenten in flammatorischen Veranderung Bei der Szintigraphie wurde eine definitiv abnormal hohe Aufnahme von $^{99}Tc^{m}DP$ bei 10 Fallen gefunden und eine wahrscheinlich zu hohe Akkumu lation bei einem von 11 mit purulenter Sinusitis Von 9 Patienten mit nicht purulenter In flammation hatten 5 eine definitiv normale und 4 eine wahrscheinlich normale Aufnahme Somit scheint es moglich zu sein zwischen einer purulenten und nicht purulenten Sinusitis mittels einer Gesichts Knochen Szintigraphie zu unterscheiden

RESUME

Dans une série de 25 malades 20 avaient un sinus maxillaire qui ne contenait pas d air a la radiographie ceci etait du dans 11 cas a une lésion inflammatoire purulente et dans 9 cas à une lesion inflammatoire non purulente A la scintigraphie on a trouve une fixation elevee nettement anormale de $Tc^{m}DP$ chez 10 malades et probablement une fixation elevee chez un des 11 malades qui avaient une sinusite purulente Parmi les 9 malades qui avaient une inflammation non purulente 5 avaient une fixation tout à fait normale et 4 une fixation probablement normale Ainsi la differenciation entre sinusite purulente et sinusite non purulente semblerait possible grace a la scintigraphie du squelette facial

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non purulent sinus inflammation in the present series (Table) Sinuses not containing air at radiography where divided by scintigraphy into four groups, two with normal and two with abnormally increased accumulation of $^{99}Tc^{m}DP$ in the region affected As the patients with purulent maxillary sinuitis all had abnormal scintigrams and the patients with non purulent inflammations all had normal scintigrams, these two groups could be distinguished by adding the results of the scintigraphy to those of radiography (Fig 3 Table)

A scintigraphic evaluation is fundamentally different from a radiologic one as it implies an aspect of bone tissue metabolic dynamics in addition to morphology (TILDEN et coll GENANT et coll KAYE et coll, ROSENTHALL & KAYE GARCIA et coll) However, non purulent inflammation with a sinus containing no air at radiography could not be distinguished from a normal sinus by scintigraphy alone (Fig 1 Table) It is thus evident that the combination of these two different methods for the evaluation of paranasal sinus affections yields more complete information than each method alone If a sinus affection is demonstrated at radiography scintigraphy can differentiate between purulent and non purulent affection However it must be emphasized that other pathologic conditions besides inflammation—neoplastic processes lesions of dental origin trauma for instance—may cause abnormal scintigraphic images of the region (BERGSTEDT & LIND)

The analysed patients had clear cut diagnoses because patients with equivocal diagnoses were excluded The patients with only marginal soft tissue swelling at radiography and those with a history of purulent inflammation but no pus on aspiration were excluded The scintigraphy results should therefore vary more in a material also including borderline cases with allergic nasal and sinus mucosal reactions sometimes complicated by purulent infections The patients with purulent sinuitis all had an abnormally high accumulation of $^{99}Tc^{m}DP$ but to a varying extent Therefore the severity of an inflammatory involvement of the bony walls of the maxillary sinus may be assessed by scintigraphy

The existence of a longstanding inflammatory reaction in a paranasal sinus demands treatment sometimes surgical Non purulent allergic reactions need not necessarily be operated upon Information obtained by facial bone scintigraphy in patients with chronic affection of the paranasal sinuses adds to the clinical radiographic and bacteriologic information and should lead to more distinct indications for surgery

SUMMARY

In a series of 25 patients 20 had a maxillary sinus not containing air at radiography in 11 due to purulent and in 9 to non purulent inflammatory lesion At scintigraphy a definitely abnormal, high uptake of $^{99}Tc^{m}DP$ was found in 10 and a probably high accumulation in one of the 11 with purulent sinuitis Of the 9 patients with non purulent inflammation 5 had a definitely normal and 4 a probably normal uptake Thus a differentiation between purulent and non purulent sinuitis would seem to be possible by means of facial bone scintigraphy

ZUSAMMENFASSUNG

In einer Serie von 25 Patienten hatten 20 einen Sinus maxillaris ohne Luft bei der Rontgen untersuchung in 11 Fallen als Folge einer purulenten und in 9 einer nicht purulenten in flammatorischen Veranderung Bei der Szintigraphie wurde eine definitiv abnormal hohe Aufnahme von Tc^{m}DP bei 10 Fallen gefunden und eine wahrscheinlich zu hohe Akkumu lation bei einem von 11 mit purulenter Sinusitis Von 9 Patienten mit nicht purulenter In flammation hatten 5 eine definitiv normale und 4 eine wahrscheinlich normale Aufnahme Somit scheint es moglich zu sein zwischen einer purulenten und nicht purulenten Sinusitis mittels einer Gesichts Knochen Szintigraphie zu unterscheiden

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RELATIONSHIP BETWEEN CLINICAL AND RADIOGRAPHIC FINDINGS IN PATIENTS WITH MANDIBULAR PAIN OR DYSFUNCTION

S KOPP and B ROCKLER

Radiography has long been the main basis for diagnosing organic diseases of the temporomandibular joint It is however often difficult to decide whether a given deviation in shape of the joint should be regarded as a normal variant or a pathologic condition (ÖBERG et coll 1971) It is likewise difficult to decide what abnormalities are characteristic of individual diseases of the joint In addition it is not easy to obtain accurate projections of this joint Tomography appears to give the most reliable information (LUNDBERG & WELANDER 1970 ECKERDAL 1973 PETERSSON 1976)

The abnormalities generally considered to be characteristic of osteoarthrosis are reduced joint space indicating loss of articular cartilage subchondral bone sclerosis due to thickening of the subchondral cortical layer and cancellous bone trabeculae and marginal osteophytes (KELLGREN & LAWRENCE 1957 AHLBACK 1968 MARTEL 1973) However it is still uncertain whether these abnormalities are characteristic of osteoarthrosis of the temporomandibular joint as well Also flattening of the condyle and the temporal eminence is a common finding in arthrosis of this joint (MADSEN 1966 ERICSON & LUNDBERG 1968 BLAIR & CHALMERS 1972 PETERSSON & NANTHAVIROJ 1975 OMNELL & PETERSSON 1976 LYSELL 1977) but may also occur in the absence of arthrosis (ÖBERG et coll)

A generalized form of osteoarthrosis has been described in association with

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Table 1

Age and sex distribution of the patients Number of patients in the age groups

Sex	Patient groups	Age (years)			Total
		16-24	25-49	50-88	
Women	Group 1	0	6	11	17
	Group 2	4	7	3	14
	Group 3	4	11	1	16
Men	Group 1	0	2	1	3
	Group 2	1	2	1	4
	Group 3	6	3	1	10

Heberden s nodes in the distal interphalangeal joints (KELLGREN & MOORE 1952 ACHESON et coll 1972) Arthrosis of the hand joints is often accompanied by arthrosis of other joints (HOAGLUND et coll 1973) and radiography of the hands has been recommended as a supplement to the radiography of the temporomandibular joint (ERICSON & LUNDBERG)

The aim of the present report is to analyse whether (1) patients with clinically diagnosed or suggested arthrosis of the temporomandibular joint differ from the rest of a patient population with respect to radiographic findings in this joint and in hand joints (interphalangeal and metacarpophalangeal joints) (2) a correlation exists between the severity of mandibular pain or dysfunction and the number of radiographic abnormalities of the temporomandibular joint and (3) any correlation could be found between the clinical findings in the masticatory system and the radiographic findings in the temporomandibular joint

Material and Method

Sixty four patients with mandibular pain or dysfunction were selected from a consecutive series of 161 referred to the Department of Stomatognathic Physiology The patients were divided into 3 groups *Group 1 consisted of patients with crepitation* in the temporomandibular joint audible with a stethoscope (n = 20) Group 2 patients with local tenderness to palpation of the joint but without crepitation (n = 18) and Group 3 (reference group) *patients without the criteria mentioned* (n = 26)

The age and sex distribution of the patients is given in Table 1 In Groups 1 and 2 the mean age was higher (55 and 36 years respectively) and women were more preponderant (85 and 78 % respectively) than in Group 3 (30 years and 62 % respectively)

Table 2

Percentage distribution of radiographic findings in the temporomandibular joint in the different groups Age is noted when correlated with the radiographic findings with a probability of p<0 4 n=64

Abnormality	Group 1	Group 2	Group 3	Test of difference between Groups 1 and 3	Test of difference between Groups 2 and 3	Correlation to age
Condyle						
Flattenin of lateral part	45	17	35			(r=0 12)
Cortical layer eroded absent	35	6	12			(r=0 20)
Subcortical sclerosis	40	17	15			(r=0 23)
Reduced mobility	37	39	42			(r=0 25)
Width of joint space						
Reduced	40	22	12	(−)		(r=0 23)
Increased	35	28	65			
Temporal eminence (oblique lateral projection)						
Flat	26	11	44			(r=−0 19)
Steep	5	6	4			
Radiographic index (0–5 units)						
0	15	44	42			
1	30	33	35			
2	30	17	8	(−)		(r=0 27)
3	20	6	12			
4	5	0	4			
Mode	2	1	1			

Radiography The temporomandibular joint of all patients was exposed in two projections (1) the oblique lateral modified after LINDBLOM (1960) (parallel with the long axis of the condyle) and (2) the transmaxillary projection according to McCABE et coll (1959) (perpendicular to the long axis of the condyle) The hands of 62 of the patients were exposed in dorso volar projection

The radiographic abnormalities of the temporomandibular joint and interphalangeal and metacarpophalangeal joints are given in Tables 2 and 3 and Figs 1 and 2 They have been described in detail previously (KOPP & ROCKLER 1978)

Indices of the radiographic findings made in the temporomandibular joint and hand joints were constructed The index of the temporomandibular joint included the following abnormalities (Table 2) flattening of the lateral part of the condyle (projection 2) flattening of the temporal eminence (projection 1) eroded or absent cortical outlining of the condyle (projection 2) subcortical sclerosis of the condyle (projection 2) reduced joint space (projection 1) The presence of any of these five

Table 3

Percentage distribution of radiographic findings of hand joints (interphalangeal and metacarpo phalangeal) in the different groups Age is noted when correlated with the radiographic findings with a probability of p<0 4 n=62 The statistical analysis is based on the number of hand joints per indivi dual afflicted with each abnormality

Abnormality	Group 1	Group 2	Group 3	Test of difference between Groups		Correlation to age
				1 and 3	2 and 3	
Osteophytes	32	0	0	(−)		(r=0 49)
Cortical layer						
Eroded/absent	16	6	0			(r=0 41)
Thickened	21	0	0	(−)		(r=0 49)
Subcortical sclerosis	32	0	0	(−)		(r=0 35)
Width of joint space						
Reduced	47	18	12	(−)		(r=0 40)
Obliterated	32	0	4	(−)		(r=0 43)
Subluxation	21	6	12			(r=0 31)
Radiographic index (0–7 units)						
0	42	82	77			
1	11	6	19			
2	16	12	4			
3	5	0	0	(−)		(r=0 41)
4	5	0	0			
5	11	0	0			
6	5	0	0			
7	5	0	0			
Mode	1	0	0			

abnormalities contributed one unit each to the score which thus varied between 0 and 5 units The radiographic index of the hand joints was constructed in the same way including all the abnormalities given in Table 3 and ranging from 0 to 7 units

Each radiographic finding in the temporomandibular joint as well as the index were analysed for any correlation with each of the clinical findings

The clinical examination of the masticatory system was performed with methods used routinely in this stomatognathic department and are described elsewhere (KROGH POULSEN 1969 CARLSSON & HELKIMO 1972) The anamnestic and clinical dysfunction indices (A_i D_i) according to HELKIMO (1974) were used as measures of the severity of mandibular pain or dysfunction The clinical examination methods used have been described in detail by KOPP (1977 b)



Fig 1 Transmaxillary projection Sclerosis of the lateral peripheral part of the temporal eminence and subcortical sclerosis in the lateral and central parts of the condyle

Statistical methods Significance tests for differences between sexes age and patient groups were performed with Fisher s permutation test (ODEN & WEDEL 1975) Significance tests for correlations were performed with Pitman s test (BRADLEY 1968) Both methods are nonparametric and are thus applicable to discrete as well as continuous distributions and give correction for ties The levels of statistical significance used for Fisher s permutation test and Pitman s test are denoted by ** $p < 0\ 01$ * $0\ 01 < p < 0\ 05$ Pearson s product moment correlation coefficient (r) was calculated to obtain an approximate estimation of the strength of the correlations containing continuous variables but no significance tests were based on this coefficient

Results

Sex and age correlations of the radiographic findings

Temporomandibular joint The radiographically demonstrated range of movement of the joint varied inversely with age ($p < 0\ 05$ Table 2) The radiographic index increased significantly with age ($p < 0\ 05$) The other single radiographic abnormalities recorded increased in frequency with age except that of flat temporal eminence which decreased These last correlations were not statistically significant ($0\ 05 < p < 0\ 40$) but age is nevertheless important as a confounding factor

Hand joints All radiographic abnormalities recorded in the hand joints as well as the radiographic index were significantly and positively correlated with age (Table 3) The strongest correlations were found for osteophytes ($p < 0\ 01$) and thickened cortical layer ($p < 0\ 01$)

None of the radiographic abnormalities varied in frequency with sex

Differences in radiographic findings between groups of patients

Temporomandibular joint A reduced joint space proved common in Group 1 (Table 4) and the difference between Groups 1 and 3 was statistically significant ($p < 0\ 05$)

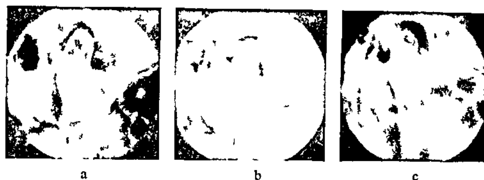


Fig. 2. Oblique lateral projection. a) Normal, b) reduced, c) increased joint space.

The radiographic index was significantly higher in Group 1 than in Group 3 ($p < 0.05$). About 55 per cent of the patients in Groups 2 and 3 had radiographic abnormalities compared with 85 per cent of Group 1. The radiographic index assumed values between 3 and 4 units for 25 per cent of the patients in Group 1 compared with 6 and 16 per cent, respectively, in Groups 2 and 3. However, the age difference between Groups 1 and 3 could not be taken into account in the statistical analysis.

Hand joints. All radiographic abnormalities were most frequently found in Group 1. Statistically significant differences between Groups 1 and 3 were found for osteophytes, thickened cortical layer, subcortical sclerosis and reduced or obliterated joint space ($p < 0.05$). The difference in radiographic index between these groups was even more marked ($p < 0.01$), but here again the difference in age between these two groups could not be taken into account. About 20 per cent of the patients in Groups 2 and 3 had radiographic abnormalities in the hand joints compared with 60 per cent in Group 1. The radiographic index assumed values between 3 and 7 units for 35 per cent of the patients in Group 1, compared with 5 and 0 per cent, respectively, in Groups 2 and 3.

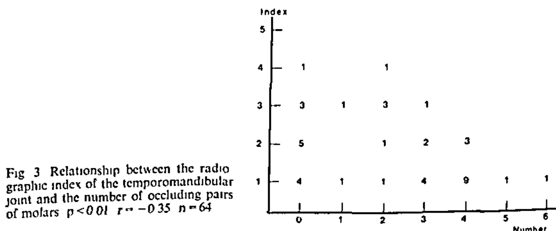


Fig. 3. Relationship between the radiographic index of the temporomandibular joint and the number of occluding pairs of molars. $p < 0.01$, $r = -0.35$, $n = 64$.

Table 4

Relationship between subcortical sclerosis of the condyle and the number of occluding pairs of molars p<0 0? r = −0.30 n = 64

Subcortical bone	Number of occluding pairs of molars				
	0	1–2	3–4	5–6	
Normal ( )	20	16	60	4	100
Sclerosed ( )	40	34	?6	0	100

Table 5

Relationship between reduced joint space of the temporomandibular joint and number of occluding pairs of molars p<0 01 r = −0 33 n = 62 (data missing for two patients due to poor quality of the films)

Width of joint space	Number of occluding pairs of molars				
	0	1–2	3–4	5–6	
Normal or increased ( )	17	19	60	4	100
Reduced ( )	53	27	20	0	100

Relationship between clinical and radiographic findings in the temporomandibular joint

Statistically significant correlations were found between the radiographic index and uni or bilateral loss of molar support (p<0 02) and the number of occluding pairs of molars (p<0 01 Fig 3) Two of the radiographic abnormalities included in the radiographic index were significantly correlated with the number of occluding pairs of molars namely subcortical sclerosis (p<0 02 Table 4) and reduced joint space (p<0 01 Table 5) However no statistically significant correlation could be found between the radiographic index and subjective or clinical dysfunction index duration of molar loss atypical attrition facets and degree of attrition

Discussion

Radiographic abnormalities of the temporomandibular and hand joints were most common in Group 1 This difference between the groups may be due to an association between crepitation and the radiographic findings or the age difference between the groups The patients in Group 1 were on the average 15 years older than those in Group 3 and the frequency of macroscopic lesions as well as radiographic arthrosis increase with age (Sokoloff 1969 Öberg et coll Acheson & Collart 1975 Kopp 1978) However crepitation has been shown to be correlated with radiographic

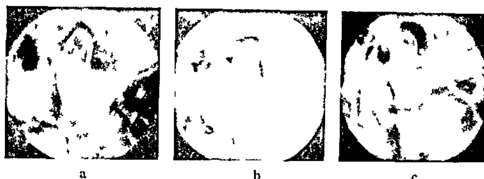


Fig 2 Oblique lateral projection a) Normal b) reduced c) increased joint space

The *radiographic index was significantly higher in Group 1 than in Group 3 ($p < 0.05$)* About 55 per cent of the patients in Groups 2 and 3 had radiographic abnormalities compared with 85 per cent of Group 1 The radiographic index assumed values be tween 3 and 4 units for 25 per cent of the patients in Group 1 compared with 6 and 16 per cent respectively in Groups 2 and 3 However the age difference between Groups 1 and 3 could not be taken into account in the statistical analysis

Hand joints All radiographic abnormalities were most frequently found in Group 1 Statistically significant differences between Groups 1 and 3 were found for osteo phytes thickened cortical layer subcortical sclerosis and reduced or obliterated joint space ($p < 0.05$) The difference in radiographic index between these groups was even more marked ($p < 0.01$) but here again the difference in age between these two groups could not be taken into account About 20 per cent of the patients in Groups 2 and 3 had radiographic abnormalities in the hand joints compared with 60 per cent in Group 1 The radiographic index assumed values between 3 and 7 units for 35 per cent of the patients in Group 1 compared with 5 and 0 per cent respectively in Groups 2 and 3

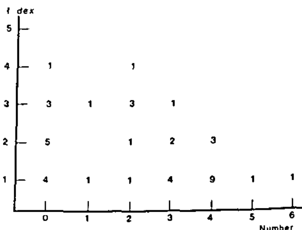


Fig 3 Relationship between the radio graphic index of the temporomandibular joint and the number of occluding pairs of molars $p < 0.01$ $r = -0.35$ $n = 64$

need not proceed to osteoarthrosis (CARLSSON et coll 1968 ÖBERG et coll CARLSSON & ÖBERG 1974)

No statistically significant difference in frequency of erosion or absence of cortical outlining of the condyle was found between the groups This corroborates the conditions in other joints where bone erosion is not a characteristic feature of osteoarthrosis but of erosive arthritis of the hand joints PETER et coll 1966 MARTEL)

Subcortical sclerosis has been claimed to indicate arthrosis (KELLGREN & LAWRENCE MADSEN MARTEL) and could be revealed in the condyle on the transmaxillary view Subcortical sclerosis of the condyle was found mainly in patients with crepitation in the joint but the difference between the groups was not statistically significant.

Several patients in Groups 2 and 3 probably had osteoarthrosis detectable at radiography but no crepitation of the joint This may explain some of the findings of eroded or absent cortical outlining subcortical sclerosis and reduced joint space in Groups 2 and 3

The predominance of radiographic abnormalities of the hand joints in patients with crepitation of the temporomandibular joint is more likely caused by age since they were relatively strongly correlated with age However periarticular swelling of the second interphalangeal joints associated with arthrosis of these joints (ACHESON et coll) has been found to be correlated with crepitation of the temporomandibular joint independently of age (KOPP 1977 b)

All radiographic abnormalities of the hand joints claimed to indicate arthrosis namely thickened cortical layer subcortical sclerosis reduced or obliterated joint space were confined to the patients with crepitation of the temporomandibular joint as well as osteophytes and eroded or absent cortical outlining Osteophytes may occur in the absence of arthrosis (DANIELSSON 1964 ÖBERG et coll HERNBORG & NILSSON 1973) The relatively frequent finding of cortical erosions may be related to a special form of arthrosis with synovitis (PETER et coll) Further experience is desirable to ascertain whether age or systemic factors are responsible for the relationship between crepitation of the temporomandibular joint and radiographic abnormalities of the hand joints

In this material no correlation was found between the number of radiographic abnormalities and degree of pain or dysfunction as measured with the different indices i e the patients with radiographic abnormality of the temporomandibular joint did not differ from the other patients with respect to degree of pain or dysfunction Epidemiologic data have shown that radiographic abnormalities in this joint are more common among individuals with symptoms or signs (joint sounds decreased mandibular movement capacity or masticatory muscles tender to palpation) than among individuals without (LYSELL 1977) A significant correlation between the severity of radiographic osteoarthrosis and the frequency of symptoms has also been found in an epidemiologic investigation by LAWRENCE et coll (1966)

The only clinical parameter correlated with the radiographic index of the temporo-

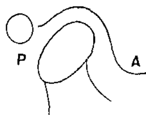


Fig 4 Shaded area indicates where the width of the joint space was estimated A = anterior P = posterior

findings in an epidemiologic investigation of 67 year old individuals (LYSELL) and crepitation is generally considered to indicate structural injury to the articular surfaces (CRAWFORD ADAMS 1971 KROGH POULSEN 1974 TOLLER 1974 KOPP 1977 a) A close correlation between crepitation and macroscopic osteoarthrotic lesions of the temporomandibular joint has also been found at operation of 200 such joints (WILKES personal communication) The most likely explanation is therefore that both crepitation and radiographic abnormalities develop as a consequence of pathologic processes in the articular tissues and therefore increase in frequency with age

Reduction of the joint space due to destruction of articular cartilage is considered to be an important radiographic indication of arthrosis in orthopaedics and rheumatology (KELLGREN & LAWRENCE MARTELL) particularly if the films are exposed during weight bearing of the joint (AHLBACK) No attempt was made to load the temporomandibular joint in this series however The width of the joint space in the present series was evaluated from the distance between the bony margin of the postero superior slope of the temporal eminence and that of the antero superior part of the condyle (Fig 4) In arthrosis the articular cartilage on these parts of the joint and the disk is gradually destroyed and becomes progressively thinner (OBERG et coll KOPP 1976) An association between reduced joint space and crepitation in the joint can therefore be expected

Loss of molar support was correlated with reduced joint space in this series and with crepitation in a previous report (KOPP 1977 b) These findings indicate that loss of molar support changes the loading of the joint and in some individuals leads to injury to the articular surface The lateral oblique projection used for estimating the width of the joint space has been claimed to be unreliable for assessing the relationship between the condyle and the temporal component at intercuspal position (PETERSSON) However, BLAIR & CHALMERS found a close agreement between circular tomography and lateral oblique radiography with respect to the position of the condyle Nevertheless determination of the joint space antero superiorly as in this series has been shown to be fairly accurate as evaluated on tomography (LUNDBERG & WELANDER) The joint space has also been shown to be relatively similar in the central and lateral parts of the joint

Abnormal shape of the temporomandibular joint was common but probably does not indicate arthrosis since such findings were made equally often in Group 3 Abnormal shape has been associated with loss of molar support (MONGINI 1972) but

fore not included in the index neither was reduced mobility of the condyle included as this condition is not specific for arthrosis of this joint

The present results demonstrate that patients with crepitation of the temporomandibular joint clinically considered as indicating arthrosis have a higher frequency of radiographic abnormalities in both this joint and in the hand joints and that age is an important factor in their development No correlation could be found between the severity of mandibular pain or dysfunction and number of radiographic abnormalities in the temporomandibular joint but loss of molar support was correlated with subcortical sclerosis of the condyle and reduced joint space

SUMMARY

The diagnosis of organic disease of the temporomandibular joint is often based on radiographic findings The relationship between the radiographic findings in this joint and in hand joints and clinical findings in the masticatory system was analysed The results showed that patients with crepitation of the temporomandibular joint frequently have radiographic abnormalities in this joint and in hand joints Subcortical sclerosis and reduced joint space were significantly correlated with the number of occluding pairs of molar teeth

ZUSAMMENFASSUNG

Die Diagnose einer organischen Erkrankung des Kiefergelenks stutzt sich oft auf rontgenologische Befunde Die Beziehung zwischen den rontgenologischen Befunden dieses Gelenks und den Handgelenken sowie den klinischen Befunden im mastikatorischen System wurde analysiert Die Ergebnisse zeigten dass Patienten mit Krepitation des Kiefergelenks oft rontgenologische Veranderungen in diesem Gelenk und im Handgelenk hatten Subkortikale Sklerose und reduzierter Gelenkspalt waren signifikant zur Anzahl von okkludierenden Paaren der molaren Zahne korreliert

RESUME

Le diagnostic d affection organique de l articulation temporo-maxillaire est souvent base sur les signes radiologiques Les auteurs ont etudie les rapports entre les signes radiographiques au niveau de cette articulation et au niveau des articulations des mains avec les signes cliniques du systeme masticatoire Les resultats montrent que les malades qui ont une crepitation de l articulation temporo maxillaire ont souvent des anomalies radiographiques de cette articulation et des articulations des mains Une sclerose souscorticale et une diminution de l interligne articulaire sont corrélees de façon significative avec le nombre des paires occlusives de molaires

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mandibular joint was loss of molar support Two variables in the index were found to be important for this correlation namely reduced joint space and subcortical sclerosis Both of them are probably the result of changed loading of the temporo mandibular joint following loss of molar support

The reduced joint space antero posteriorly (Fig 4) may be due to an antero posterior displacement of the condyle or destruction of the articular cartilage or both A destruction is more probably the explanation when the reduced joint space is associated with crepitation However, reduced joint space is probably not a radio graphic indication of arthrosis of the joint if molar support is present and the films are exposed with the mandible in the intercuspal position This condition may explain at least in part the relatively high proportion of patients with crepitation and normal or *increased* joint space *in the* present series Efforts should therefore be made to perform the radiographic examination with the functional articular surfaces of the joint in contact, i e with the mandible in a slightly protrusive or laterotrusive posi tion (OMNELL & LYSELL 1974) The subcortical sclerosis is most probably a response to increased functional demand following loss of molar support and this abnormality has been shown to disappear in the hip joint after osteotomy (OLSSON 1974)

All the radiographic abnormalities of the temporomandibular joint recorded ex *cept one increased in frequency with age, although the correlation with age was* statistically significant only for reduced mobility of the condyle and for the radio graphic index The correlation with age was stronger for the radiographic abnormali ties of the hand joints which probably means that age is a more important factor for the development of arthrosis of the hand joints than for that of the temporo mandibular joint No statistically significant difference between the sexes was found for any of the radiographic abnormalities or indices although the number of men was *small The age and sex distributions of radiographic findings considered as indicating* arthrosis in the present series corroborates those found in epidemiologic investiga tions of the temporomandibular joint (HELOE & HELÖE 1975 LYSELL) as well as of hand joints (ACHESON & COLLART)

The observer variability in the evaluation of the radiographic findings has been analysed previously (*KOPP & ROCKLER 1978) and those with the widest range of* variation were not included in the present report

The osteolysis demonstrated as eroded or absent cortical layer is most characteristic of inflammatory disease However serologic tests for the rheumatoid factor were performed in the patients with recurrent pain or swelling of peripheral joints Patients with positive tests were excluded from the present material as were all patients with known systemic disease of the muscles and joints A steep temporal eminence was not included *in the radiographic index because it was so rarely demonstrated* Increased width of the joint space as measured in the present series may be caused by an inferior or posterior displacement of the mandibular condyle due to a disturbance of the occlusion or to an increased amount of joint fluid But neither of these condi tions is directly related to arthrosis of the temporomandibular joint and was there

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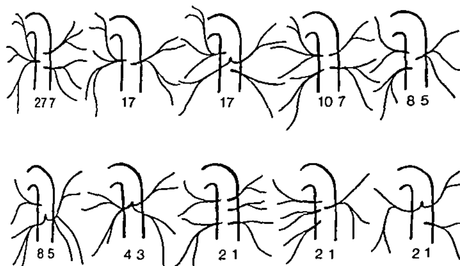


Fig 1 Anatomic variations of the bronchial arteries The figures represent percentages derived from the material of BOTENGA Accessory and aberrantly arising bronchial arteries excluded

Material

The material consisted of 47 patients (40 males 7 females) aged between 47 and 75 years (median 63 years) According to the TNM classification (UICC 1974) 14 patients had local disease stage II while 33 had more extensive disease The procedure (selective bronchial or intercostal angiography with infusion of MMC) was successfully carried out in 39 patients but the tumor feeding artery was not found in 8 patients in 6 on the left and in 2 on the right side

Anatomy

Bronchial arteries The anatomy of the bronchial arteries based on autopsy dissection has b en described in great detail by NAKAMURA (1924) LIEBOW et coll (1965) and CAULDWELL et coll (1948) The angiographic anatomy has been thoroughly presented by BOTENGA (1970)

The following description is based on these reports The right bronchial artery usually arises together with a right intercostal artery most commonly the third As a rule the left bronchial arteries arise directly from the descending aorta Though the site of origin may range from the level of vertebrae Th4 to Th9 more than 90 per cent of all bronchial arteries arise opposite to Th5 and Th6 and in a specific patient the area of origin usually is even more limited

In approximately two thirds of all cases one intercostobronchial trunk exists on the right side and one or two bronchial arteries on the left side arising directly from

FROM THE DEPARTMENT OF DIAGNOSTIC RADIOLOGY MALMÖ ALLMANNA SJUKHUS, S 214 01 MALMÖ, SWEDEN

BRONCHIAL ANGIOGRAPHY AND INTRAARTERIAL CHEMOTHERAPY WITH MITOMYCIN C IN BRONCHOGENIC CARCINOMA

Anatomy, technique, complications

CHRISTER HELLEKANT

Several attempts have been made with intraarterial infusions of cytostatic drugs in order to improve the prognosis of bronchial carcinoma In the beginning these infusions were made into the aorta at the level of the bronchial arteries Later balloon catheters were used to limit the area of perfusion (SODERBERG et coll 1964 CLIFFTON 1969)

With the development of selective bronchial angiography local intraarterial perfusion became possible and different drugs were tested (BOIJSEN et coll 1964 KAHN et coll 1965 HALLER et coll 1966 NORDENSTRÖM 1966 TATE et coll 1968 WIRTANEN & ANSFIELD 1968) both as single infusions and with indwelling catheters Little improvement if any was achieved and the technique was abandoned partly because of the unsatisfactory result partly because of the side effects sometimes severe (FEIGELSON & RAVIN 1965 RHEINLANDER et coll 1966 DI CHIRO et coll 1967 STECKEL et coll 1967 RÉMY et coll 1968)

At this department intraarterial infusion of mitomycin C (MMC) has been tested since December 1975 in patients with bronchogenic carcinoma The preliminary results were recently reported (*HELLEKANT et coll 1978*) *In the present report* the pertinent anatomy and the technique used are described and possible reasons for complications discussed

Submitted for publication 8 June 1978



Fig 3 Large spinal artery (→) arising from the 5th right intercostal artery Typical hair pin shape

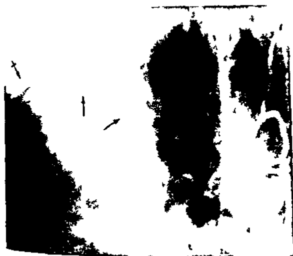


Fig 4 Bronchogenic carcinoma Right bronchial angiography lateral view Retrograde filling of small aberrant bronchial artery (→) arising from the internal mammary artery (+→)

Spinal arteries A comprehensive description of the angiographic anatomy is given by DJINDJIAN et coll (1970) and most of the following description is derived from that work

The spinal cord is supplied by *one larger anterior and two smaller posterior* spinal arteries running along its surface from the infrabulbar region down to the conus terminalis

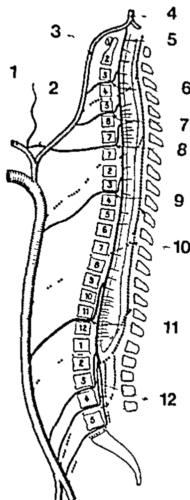


Fig 2 Arterial supply to the spinal cord 1 Subclavian artery 2 Deep cervical artery 3 Vertebral artery 4 Basilar trunk 5 Anterior spinal artery 6-9 Spinal branches 10 Posterior spinal artery with supplying spinal branches 11 Artery of Adamkiewicz 12 Lumbosacral spinal branches (After DJINDJIAN et coll Courtesy of Masson & Cie Paris)

the aorta but the variations are manifold particularly on the left side The different combinations as derived from BOTENGA, appear in Fig 1

The bronchial arteries arising directly from the aorta usually have a ventral or ventrolateral origin and run off perpendicular to the aortic wall while the intercostobronchial trunks arise laterally or dorsolaterally and have a more upward direction

Bronchial arteries rarely arise from the aortic arch or from other arteries in the greater circulation such as the internal mammary artery the pericardiophrenic the inferior phrenic the thyreocervical the left subclavian and the innominate artery or the abdominal aorta

Apart from the bronchi and the peribronchial connective tissue the bronchial arteries also supply parts of the trachea the esophagus the prevertebral muscles the vagus nerve, the visceral pleura and the parietal leaf of the pericardium They also supply tracheal, superior and inferior tracheobronchial and pulmonary lymph nodes and give off vasa vasorum to the aortic arch and the pulmonary arteries and veins



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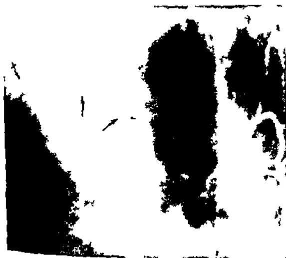


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The spinal cord is supplied by one larger anterior and two smaller posterior spinal arteries running along its surface from the infrabulbar region down to the conus terminalis

The anterior spinal artery originates from branches from the vertebral arteries and receives blood at several levels from a number (usually 6–8) of radiculomedullary arteries or spinal branches arising from the subclavian intercostal lumbar, and ileosacral arteries (Fig 2) The number and site of origin of these spinal branches vary The largest the most important and constant is the artery of Adamkiewicz which usually arises from a left intercostal or lumbar artery between the levels of Th9 and L2 most commonly between Th9 and Th12 However, it may have a higher origin from the 5th, 6th or 7th intercostal arteries (FAURE et coll 1967, KARDJIEV et coll 1974)

The other spinal branches are smaller but occasionally a larger one is present supplying the upper and middle third of the thoracic cord Such arteries have been demonstrated by BOTENGA arising from the 2nd to the 4th intercostal artery on both sides

All spinal branches arising from segmental arteries have the shape of an inverted V (hairpin shape) with a narrow ascending branch going upwards along the cord and a considerably wider branch going downwards (Fig 3)

These ascending and descending branches anastomose with corresponding branches of higher and lower spinal branches forming the anterior spinal artery

The posterior spinal arteries are formed in a similar way and derive from numerous spinal branches usually between 10 and 23 Some of these spinal branches have origins common with those supplying the anterior spinal artery, some have separate origins

Although the anterior and posterior spinal arteries run along the entire spinal cord their lumina occasionally are very narrow or even discontinuous Therefore, a sufficient circulation cannot always be maintained in case of blocking of one of the larger segmental contributors

Comments A detailed demonstration of the angiographic anatomy of the bronchial arteries demands an extensive and time consuming examination The present intention was mainly to demonstrate the tumor supply and to infuse cyto statics A discussion on the frequency of different anatomic variations can therefore not be given but a few points will be emphasized

The diameter of the normal bronchial artery is approximately one or 2 mm but when supplying a tumor or an inflammatory lesion it is often wider Despite that the anatomy of the bronchial artery varies widely the tumor feeding artery is usually found opposite the level of Th5 to Th6 The aberrant arteries are usually small and of accessory character supplying structures in the vicinity of the hilum and are of minor importance from the present point of view

Catheterization of arteries known to give off aberrant bronchial arteries was not routinely tried but small branches communicating with the internal mammary and the thyreocervical arteries have been demonstrated by filling in a retrograde direc tion after injection into bronchial arteries (Fig 4)





a Fig 5 b

Fig 5 Central bronchogenic carcinoma Left bronchial angiography a) A p b) lateral view Large tumor feeding artery (↠) and small branches supplying the aortic arch (→)



Fig 6

Fig 6 Bronchogenic carcinoma Left bronchial angiography Network of vasa vasorum along the left wall of the descending aorta (→) Large draining vein belonging to the hemiazygos system (↠)

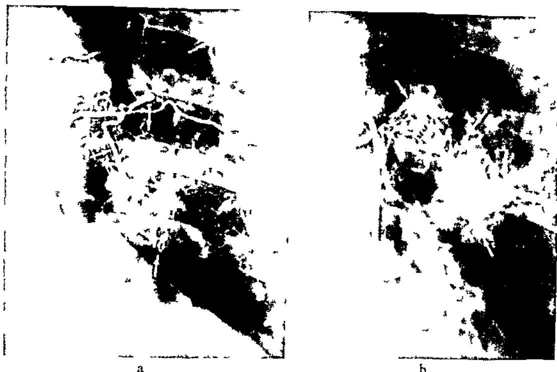


Fig 7 Centrally located bronchogenic carcinoma a) Injection into the 4th intercostal artery Dorsal muscular branch (↔) superimposed but not supplying the tumor b) Injection into the bronchial artery Arterial branches along the bronchus and filling of tumor (→)

In accordance with BOTENGA filling of vasa vasorum of the aorta was frequently observed when a left bronchial artery was examined These small vessels were demonstrated whenever a single or upper left bronchial artery was injected but never from the lower of two left arteries

At bronchial angiography on the left side aortic branches were demonstrated in 10 of 19 patients In the remaining 9 patients the upper left bronchial artery had probably not been examined

The appearance of the vasa vasorum varied from very small branches running along the aortic arch (Fig 5) to a network of vessels covering a large area along the aortic arch and the left wall of the descending aorta No filling of these vessels occurred from bronchial arteries on the right side In most cases also the draining vein belonging to the hemiazygos system was demonstrated (Fig 6)

No convincing reports have appeared documenting a left intercostobronchial trunk, except in patients with situs inversus but a left bronchial artery may arise from a right intercostobronchial trunk (CAULDWELL et coll)

A bronchial artery arising from a left intercostobronchial trunk has been described and illustrated by MILNE (1967) and by NORDENSTRÖM (1967) However the vessel described seems to represent a dorsal muscular branch such a branch may be difficult to distinguish from a bronchial artery if only one projection is used (Fig 7)

Spinal feeding arteries are rarely observed at bronchial angiography BOTENGA reported filling of the anterior spinal artery in 6 of 143 selective bronchial angiographies In the present material one large spinal trunk was encountered arising from the 5th right intercostal artery its typical shape facilitated prompt recognition (Fig 3)

The posterior spinal arteries are much narrower than the anterior ones and according to DJINDJIAN et coll they are rarely visible in a p projection unless widened

Angiographic technique

The aortic level opposite vertebra Th5 is identified on a pa chest film and is usually located just above the left main bronchus In elderly patients it may be located considerably higher due to increased kyphosis with concomitant bending of the aorta

Angiography is performed percutaneously via the femoral artery using a catheter (Surgimed Denmark) with OD/ID 2 2/1 45 mm The distal 2 cm of the catheter is tapered to OD/ID 1 4/1 0 mm and the catheter bent as illustrated in Fig 8 (upper view)

On the right side the artery supplying the 2nd and 3rd intercostal space is sought and in searching for the left bronchial arteries the ventral wall of the aorta at the level of Th5 and Th6 is gently probed by moving the tip of the catheter in small zig za motions over the surface

When an artery is entered one to 2 ml of contrast medium is injected (Isopaque Cerebral 280 mg I/ml Nyegaard Norway) but only if aspiration of blood is possible through the catheter

When the proper tumor feeding artery has been catheterized angiography is performed using 3 to 5 ml of contrast medium injected at a rate of 2 to 3 ml/s by hand or by an automatic injection pump depending on the size of the artery and the stability of the catheter position Films are exposed at a rate of 2/s for 4 s and 1/s for another 4 s First an a p series is exposed When these films have been scrutinized for a spinal artery the patient is turned to a lateral position and a similar series is exposed Frequently the a p series is repeated with a larger dose of contrast medium (5-10 ml)

At the end of the examination a film is exposed over the kidneys because they are fairly commonly the site for metastases from pulmonary carcinoma

Comments To obtain a complete information of all bronchial arteries is very time-consuming but the interest of this investigation has been limited to the tumor feeding artery This artery is often easy to catheterize due to its wider caliber Therefore the angiography was generally completed within one hour

BOTENGA recommended different catheters for the right and left bronchial arteries the catheter for the right side having a tip directed more cranially to fit the

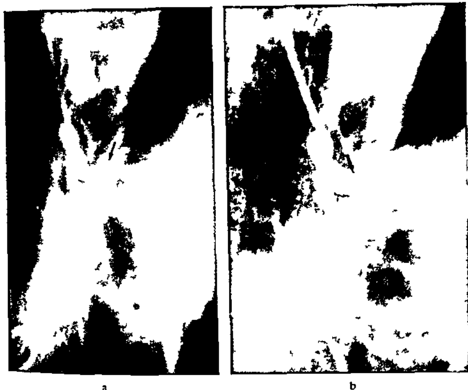


Fig 8 Catheters used for bronchial angiography Approximately ⅔ of original size Top Standard shape for right and left side Bottom Catheter suitable for arteries with more perpendicular take off from the aorta

anatomy of the intercostobronchial trunk As a rule this trunk has this direction in younger patients while in elderly the proximal part of the intercostobronchial trunk often has a more downward course (Fig 9) The tip of the catheter used in the present series can be directed either cranially or caudally thus making different catheters unnecessary The proximal bend furthermore stabilizes the catheter against the opposite wall preventing recoil during injection When the bronchial artery has a perpendicular course from the aorta it is sometimes easier to obtain a stable catheter position using a catheter bent as illustrated in Fig 8 (lower view) In patients with very tortuous iliac vessels or an elongated aorta a Cook catheter designed by Judkins for the right coronary artery may be used It gives maximum torque control making catheterization possible also in patients with severe athero sclerosis

Bronchial arteries arising high near the vertex of the arch, were difficult to catheterize from the femoral artery but catheterization was made possible in most cases if the catheter was given a more acute proximal bend as estimated from the shape of the aorta on a lateral chest film

Intercostal and large bronchial arteries were easily recognized on the monitor during test injection while small branches could be difficult to indentify without radiography When an intercostal artery was injected the patient experienced a burning pain in the muscles in the back while injection into a bronchial artery often gave a burning sensation in the throat sometimes accompanied by an urge to



a b

Fig. 9 Right bronchial angiography a) Catheter with tip directed upwards (→) cannot enter the intercostobronchial trunk which has a downward course from the aorta b) With tip directed downwards (→) a catheter position suitable for drug infusion is obtained

cough The burning is probably caused by contrast medium passing through small branches supplying the middle third of the esophagus (Fig 10)

A rich tumor vascularity usually confirms that the tumor feeding artery has been injected but it must be emphasized that the tumor may be supplied by more than one bronchial artery especially on the left side A dual supply should be considered whenever marginal defects are found in the tumor vascularity

Different opinions exist about the vascular supply of pulmonary tumors (WRIGHT 1938 CUDKOWICZ & ARMSTRONG 1953 MILNE) On the basis of post mortem angiography MILNE concluded that primary tumors have a predominant bronchial circulation but that a pulmonary artery component is present in many cases the more peripheral the site of the tumor the more common is the pulmonary artery component

Most of the present tumors were centrally located but the material also comprised peripheral tumors All tumors received blood from the bronchial arteries but some of the peripheral ones in addition received blood from other systemic arteries such



Fig 10 Right bronchial angio graphy Lateral view Arterial sup ply to the middle third of the eso phagus (→) explaining burning sensation in the throat during an giography

as the *subclavian the internal mammary intercostal or inferior phrenic* arteries In no case was any vascular supply from the pulmonary arteries demonstrated at selective pulmonary angiography

If no tumor feeding artery is found within reasonable time it may be of value to perform aortography with the catheter at the level of the left subclavian artery and the patient in a prone or lateral position NORDENSTRÖM (1967) suggested aorto graphy *routinely before selective bronchial angiography but this appears to be* unnecessary in most cases

The tumor feeding artery was not found in 8 of 47 patients in only one of these eight it was found following aortography Five of the failures occurred early in the series and were apparently caused by insufficient experience The remaining 3 occurred in patients over 70 years of age and with extensive atherosclerosis

Infusion of mitomycin C

After angiographic identification of the tumor supply 10 mg MMC diluted in 100 ml physiologic saline were infused into the feeding artery at a rate of 6 ml/min using an automatic infusion pump (Mark IV Medrad U S A) The position of the tip of the catheter was frequently controlled fluoroscopically A three way stop cock



Fig 11 Inoperable squamous cell carcinoma of the left lung a) Chest film before infusion b) Day after intraarterial infusion of 10 mg MMC Tumor appears larger and is surrounded by a pneumonic infiltrate also pleural effusion present

between the pump and the catheter made injection of contrast medium possible without disconnecting the system

The patients were treated between one and 5 times the intervals ranging from one to 8 weeks The effect of the therapy was recorded by clinical examination spirometry ^{133}Xe spirometry bronchoscopy and repeated chest films White blood cells and thrombocytes were determined in all patients once a week after the first infusion

Side effects During angiography the patients routinely experienced a moderate burning sensation in the throat or in the chest When examining arteries on the right side communicating with muscular branches in the neck or in the back the pain usually was more intense but it still lasted only 5 to 10 seconds

No side effects were registered during the infusion of MMC except coughing in 3 patients Many patients had a slight elevation of temperature the day after the infusion and some patients also had a moderate malaise The white blood cells or thrombocytes were not significantly reduced More severe side effects occurred in 3 patients A 72 year-old male with an inoperable squamous cell carcinoma of the left

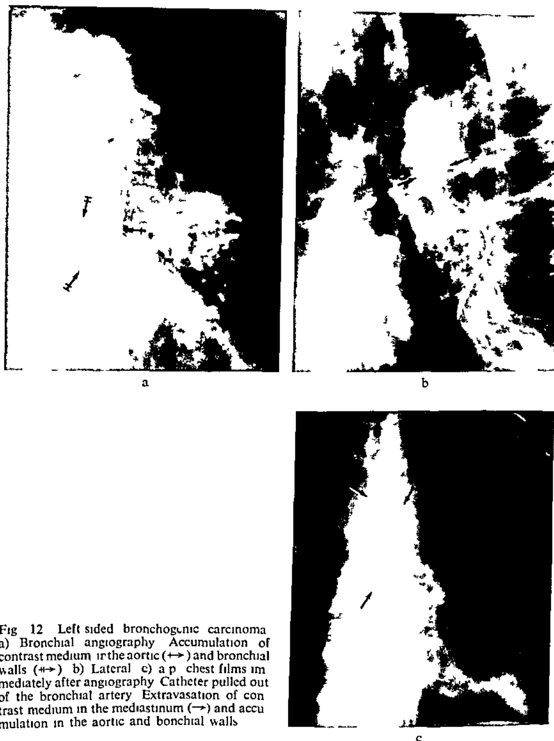


Fig 12 Left sided bronchogenic carcinoma a) Bronchial angiography Accumulation of contrast medium in the aortic (↔) and bronchial walls (⇸) b) Lateral c) a p chest films immediately after angiography Catheter pulled out of the bronchial artery Extravasation of contrast medium in the mediastinum (→) and accumulation in the aortic and bonchial walls

lung complained of intermittent claudication of his left limb after a catheterization performed 3 weeks previously from the left femoral artery At a repeat infusion the right femoral artery was used An injection of contrast medium revealed an occlusion of the left external iliac artery just above the inguinal ligament The patient developed

fever and pneumonia after 2 of 3 infusions and chest films demonstrated a parenchymal infiltration around the tumor and a small left sided pleural effusion (Fig 11) considered to be caused by a chemical pneumonia These abnormalities disappeared after treatment with antibiotics

A similar chemical pneumonia was observed in another patient after the first of 5 infusions but in connection with the following 4 infusions no side effects occurred

In a 6? year old female with an adenocarcinoma of the left lung bronchial angiography demonstrated a richly vascularized tumor The bronchial artery made a sharp turn just distal to the tip of the catheter An infusion of MMC was performed without any side effects and a slight reduction of the size of the tumor was observed on subsequent chest films Six weeks later the bronchial artery was more difficult to catheterize and aspiration of blood from the artery was slower than expected A test injection demonstrated a patent artery and angiography was performed At fluoroscopy after the angiography extravasation of contrast medium to the mediastinum was observed and the catheter immediately withdrawn A marked accumulation of contrast medium in the bronchial tracheal and aortic walls was observed on subsequent films (Fig 12) The patient had no immediate complaints but during the following hour she developed a burning pain in the mediastinum lasting for 24 hours No other symptoms occurred and repeated chest films did not reveal any further pathology At repeat angiography 10 days later the bronchial artery was occluded corresponding to the kinking observed at the first angiography

Comments Every angiography carries a certain risk of arterial injury such as thrombosis and dissection of the intima especially in elderly patients The risk of thrombosis is among other factors proportional to the duration of the catheterization (JONSSON et coll 1977 FORMANEK et coll 1970) Therefore intermittent short term infusions of cytotoxic drugs seems preferable to long term infusions with indwelling catheters as reported by others (KHAN et coll WIRTANEN & ANSFIELD)

With the present method the procedure (angiography and drug infusion) is usually completed within one hour and a half and even faster at repeat infusions when the anatomy is known

Selective catheterization of small vessels increases the risk of injury to the intima but should be possible to avoid with a careful technique It is possible that the complication encountered in the third of the reported cases partly was caused by weakening of the wall due to the previous infusion of MMC

Apart from these general risks selective bronchial angiography carries the risk of neurologic complications (FEIGELSON & RAVIN KARDJIEV et coll RÉMY et coll) The common factor in these cases seems to have been an injection of a highly concentrated contrast medium into an artery supplying the spinal cord An unintentional injection of a large amount of contrast medium into an artery feeding the cord may cause severe injury with irreversible paraplegia (BROY 1971) Transient paresis and

other neurologic disturbances have been reported after injection of as little as one to *5 ml of a highly* concentrated contrast medium into the 5th right intercostal artery (FEIGELSON & RAVIN REMY et coll KARDJIEV et coll) A probable explanation is found in the *statement of* KARDJIEV *et coll that total occlusion of the vessels* was achieved in nearly all patients (during angiography) and the same mechanism probably caused the similar complications reported by the other authors

In the beginning of the present series 10 ml of contrast medium were unintentionally injected into a 5th right intercostal artery, from which a fairly large spinal artery arose (Fig 3) The patient experienced a burning sensation along the spine but no neurologic symptoms or signs occurred

A temporary occlusion of an artery to the spinal cord during angiography prevents dilution of the contrast medium by blood and lengthens the time of contact between *the medium and the elements of the blood brain barrier Thus the risk of injury is* increased The significance of a correct technique was emphasized by DJINDJIAN et coll who encountered paroxysmal muscular contractions in 9 patients in a series of 240 selective angiographies of the spinal cord but no fatal complications Apart from the amount injected also the type and concentration of the contrast medium are of importance Experimental and clinical experiences indicate that modern ionic media and especially their meglumine calcium salts are less neurotoxic than older contrast media (MARGOLIS & YERASIMIDES *1966* DI CHIRO *1974* SALVESEN et coll 1967) but the non ionic metrizamide (Amipaque Nyegaard Norway) has an even *lower neurotoxicity than other media presently in clinical use* (SALVESEN 1973 a, b) If the lumen of the catheterized artery is not occluded complications from contrast media should be improbable On the basis of these experiences it is advisable to use a tapered catheter thin enough to allow a certain blood flow into the catheterized vessel and to make sure that aspiration is possible before injection of contrast medium

It is also suggested to use a medium containing less than 300 mg I/ml which has an adequate attenuation capacity for demonstration of the bronchial arteries

Should the patient experience pain along the spine or muscular contractions in the abdomen or in the legs indicating that an artery running to the spinal cord has been injected the catheter should be withdrawn immediately If the contractions persist a selective injection of 5 mg Valium into the artery to the cord is recommended (DJINDJIAN et coll) The attack then usually ceases immediately In case of an injury to the cord the paresis usually does not develop until one to two hours after the injection (KARDJIEV et coll) In such a case a spinal lavage has been suggested with *replacement of spinal fluid by physiologic saline* (*DI CHIRO* MARGOLIS 1976)

Previous reports on local complications associated with intraarterial infusion of cytostatic drugs in experimental animals and in humans include chemical pneumonia (SODERBERG et coll MARK et coll 1965) pleural effusion (CLIFFTON & MAHAJAN 1963) thrombosis of the bronchial artery (KAHN et coll) bronchial and esophageal ulcers (MARK et coll) and vascular injury (HOCKMAN et coll 1964)

STECKEL et coll reported a case of aortic rupture after injection of nitrogen mustard into a left bronchial artery and the anatomic background to such a complication was demonstrated in several of the present patients (Figs 5 6 12)

When the bronchial blood flow was markedly impaired by the position of the catheter a longstanding accumulation of contrast medium in the aortic wall was occasionally observed This again emphasizes the importance of using a catheter thin enough to allow blood flow into the bronchial artery during infusion of the cyto static drug for avoiding local vascular injury

MMC was chosen as cytostatic agent as it is well tolerated presumably effective during the whole cell cycle and has a well documented effect in pulmonary carcinoma (WASSERMAN et coll 1975) It has furthermore been shown to accumulate in malignant tissue more than in normal tissues even after intravenous administration It is mainly inactivated in the liver spleen kidneys brain and heart (FUJITA 1971) A direct infusion into the tumor feeding bronchial artery should therefore increase its effectiveness on the malignant cells

Undiluted MMC is highly toxic and may cause local vascular or tissue necrosis but by diluting the drug this risk should be eliminated

The most significant systemic toxicity of MMC is myelosuppression FRANK & OSTERBERG (1960) concluded that in 67 per cent of responding and in 40 per cent of non responding patients hematopoietic toxicity was evident after intravenous administration The toxicity was directly related to the dose and rarely occurred below a total dose of 40 mg Similar figures have been reported by VAN DER MERWE & FALKSON (1971)

Most of the present patients were given 10 to 20 mg totally but 30 to 50 mg were administered to 5 patients In no case was any hematopoietic toxicity observed

SUMMARY

Bronchial angiography and intraarterial infusion of mitomycin-C were successfully performed in 39 of 47 patients with bronchogenic carcinoma More than one course was given to several patients No neurologic complications occurred and the side effects were insignificant The pertinent anatomy of the bronchial and spinal arteries is summarized and a comprehensive description of the angiography and infusion technique is given It is important that the infused artery is not occluded by the catheter and that the drug is properly diluted to avoid complications The method appears to be of therapeutic value in the treatment of pulmonary carcinoma

ZUSAMMENFASSUNG

Bronchiale Angiographie und intraarterielle Infusion von Mitomycin C wurden erfolgreich bei 39 von 47 Patienten mit bronchogenem Karzinomen durchgeführt Verschiedenen Patienten wurde mehr als eine Kur gegeben Es traten keine neurologischen Komplikationen auf und die Nebeneffekte waren gering Die relevante Anatomie der bronchialen und spinalen Arterien werden zusammengefasst und eine umfassende Beschreibung der Angio-

other neurologic disturbances have been reported after injection of as little as one to 5 ml of a highly concentrated contrast medium into the 5th right intercostal artery (FEIGELSON & RAVIN, REMY et coll KARDJIEV et coll) A *probable explanation is* found in the statement of KARDJIEV et coll that total occlusion of the vessels was *achieved in nearly all patients* (during angiography) and the same mechanism probably caused the similar complications reported by the other authors

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graphie und der Infusionstechnik gegeben Es ist wesentlich dass die infundierte Arterie nicht durch den Katheter verschlossen wird und dass die Substanz ordentlich verdunnt wird um Komplikationen zu vermeiden Die Methode scheint von therapeutischen Wert bei der Behandlung von Lungenkarzinomen zu sein

RESUME

L auteur a réalisé avec succès une angiographie bronchique et une perfusion intra *artérielle de mitomycine C chez 39 malades sur 47 atteints de cancer bronchique* Plusieurs malades ont eu plus d une perfusion intraarterielle L auteur résume l anatomie des artères bronchiques et spinales et donne une description détaillée de la technique d angiographie et de perfusion Il est important que l artere perfusée ne soit pas obstruée par le cathéter et que le medicament soit convenablement dilué pour éviter des complications Cette methode semble avoir un intéret thérapeutique dans le traitement du cancer du poumon

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FROM THE DEPARTMENT OF NUCLEAR MEDICINE THE RADIUM STATION ÅRHUS MUNICIPAL HOSPITAL DK 8000 ÅRHUS DENMARK

COMBINED VENTILATION PERFUSION SCINTIGRAPHY FOR DEMONSTRATION OF PULMONARY EMBOLISM

J KIIL and F TAAGEHØJ JENSEN

Evaluation of prophylactic measures against pulmonary embolism requires reliable diagnostic methods Pulmonary perfusion scintigraphy without perfusion defects rules out pulmonary embolism (POULOSE et coll 1970) However perfusion defects may be produced by conditions causing decreased ventilation in a lung section with a consequent reduction of blood flow but without direct vascular obstruction (LOPEZ MAJANO et coll 1966 ISAWA et coll 1967) Thus the test appears to offer a high degree of diagnostic sensitivity but a lower diagnostic specificity (WULFF 1976)

Curiously enough pulmonary embolism does not seem to cause reduced ventilation of the affected region (DENARDO et coll 1970 WILLIAMS et coll 1974) The combination of perfusion scintigraphy with ventilation scintigraphy thus seems to make possible a differentiation between perfusion defects due to vascular obstruction and those secondary to obstruction in the bronchial system Therefore an investigation was performed to analyse whether the combination of perfusion and ventilation scintigraphy would improve detection of pulmonary embolism in patients with clinical symptoms suggesting this condition over that achieved by use of perfusion scintigraphy alone

Material and Methods

Over a two year period 34 patients with possible pulmonary embolism were referred for scintigraphy Twenty two patients had symptoms of acute pulmonary

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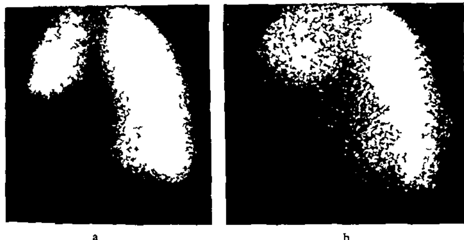


Fig. 2 a) Perfusion scintigraphy Patient with atelectasis in the right lower lobe No perfusion through the affected lobe Anterior projection b) Ventilation scintigraphy Same case as in (a) No ventilation in the affected lobe

positioned images were produced using the same apparatus recording 100 000 counts in each position Fig 1 b demonstrates the perfusion scan from the same normal subject as in Fig 1 a

The radiation dose to the patient from these two scintigraphic examinations was approximately 6 mGy (600 mrad) to the lungs and approximately 0 06 mGy (6 mrad) to the gonads

Scintigraphic evaluation Ventilation and perfusion images were assessed independently The result was considered normal if the activity in both lung compartments was uniformly distributed Well defined defects corresponding to one or several segments were regarded as an indication of ceased ventilation or perfusion Comparing the results from the two examinations the patients were classified into three groups (a) normal with both methods (b) similar defects with both methods and (c) isolated defects with one of the methods only

Phlebography Ascending phlebography of the leg was performed via a dorsal foot vein using the technique described elsewhere (KIIL & MØLLER 1979) with the sole object of determining whether thrombi existed in the femoral or iliac veins The phlebography was performed in close relation to the scintigraphy

Confirmation of pulmonary embolism Clinical symptoms suggesting pulmonary embolism formed the criterion for the inclusion of patients in the series The diagnosis

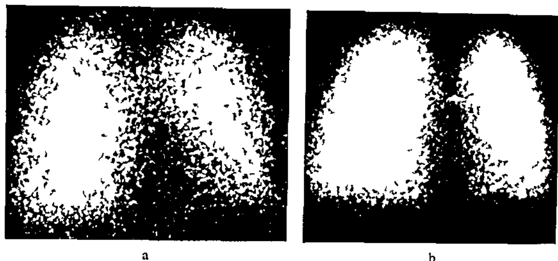


Fig 1 a) Ventilation scintigraphy with ^{133}Xe Normal subject Anterior projection b) Perfusion scintigraphy with ^{99}Tc^{m} labelled macro aggregated albumin Same subject as in (a) Anterior projection

embolism with dyspnoea cyanosis and chest pains Two patients were examined a few weeks after pulmonary embolectomy and 10 because of gradually developing dyspnoea and coughing One of these had been examined a few months previously because of acute pulmonary embolism, an embolus was demonstrated in the right upper lobe In one patient normally ventilated perfusion defects were present in one lung and a combined ventilation perfusion defect in the other lung The results from each lung have been considered separately Thus, a total of 35 examinations were performed in 33 patients

In 16 patients the symptoms of pulmonary embolism occurred postoperatively

Ventilation scintigraphy was carried out before perfusion scintigraphy The patient breathed into a spirometer (Godart expirograph type EP 6200) containing 10 l atmospheric air with 0 74 GBq (20 mCi) ^{133}Xe (AB Atomenergi Studsvik Sweden) via a mask (McKessen or Warne) covering the nose and mouth The patient was placed in the supine position and instructed to breathe normally Images were recorded anteriorly from the left and right sides and if possible from the rear with the patient in a sitting position

Analogue scintigraphic images were produced by a gamma camera (Pho gamma III, High Performance with a 16000 hole divergent collimator Searle Radiographic) recording 50 000 counts in each position Fig 1 a illustrates the results from a normal subject

Perfusion scintigraphy After conclusion of ventilation scintigraphy 37 MBq (1 mCi) ^{99}Tc^{m} macro aggregated albumin (Hoechst) was injected intravenously Identically

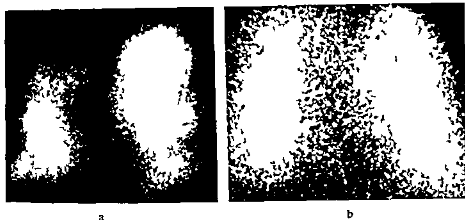


Fig 3 a) Perfusion scintigraphy Patient with pulmonary embolism Several defects in both lungs Anterior projection b) Ventilation scintigraphy Same case as in (a) No defects

of the calf veins was demonstrated at phlebography but no thrombi were found in the femoral or iliac veins

One of the 4 patients in whom phlebography was not performed for technical reasons had in addition to dyspnoea and pain in the thorax swelling and soreness of one leg localized to the crus In 10 of the 12 patients only one scintigraphy was performed In 2 the examination was repeated a few days after the symptoms had decreased An isolated perfusion defect had then disappeared

Perfusion scintigraphy Perfusion defects with or without ventilation defects were demonstrated in 33 patients Presence of pulmonary emboli was confirmed or probable in 10 of these patients and absence in 11 patients In the remaining 12 patients the presence or absence of emboli could not be established Examples of perfusion defects are illustrated in Figs 2 a and 3 a

The absence of emboli was confirmed in 2 patients without perfusion defects

Thus in 23 patients examined with perfusion scintigraphy pulmonary emboli had been confirmed as present or absent The calculation of diagnostic specificity and sensitivity based on these 23 appears in Table 1

Combined ventilation and perfusion scintigraphy In 2 patients the findings were normal and pulmonary emboli were shown to be absent in both of them

Twelve of the 33 patients with perfusion defects also had ventilation defects No pulmonary emboli were found in 11 of these patients but could not be definitely excluded in the remaining cases An example of combined ventilation and perfusion defects is given in Fig 2 from a patient with a bronchial obstruction

In the 21 patients with perfusion defects only the diagnosis of pulmonary emboli was confirmed or considered probable in 10 cases but could not be established in the

was considered definite if emboli were found in the pulmonary arteries or peripheral branches at autopsy or surgery The diagnosis was considered probable if thrombosis of the iliac or femoral veins was demonstrated by phlebography

No emboli found in the pulmonary artery branches at autopsy was considered to be absence of pulmonary embolism Bronchoscopically identified bronchial obstruction was considered to be a criterion of a perfusion defect being secondary to ceased ventilation and not due to pulmonary embolism

In some patients no confirmation was obtained by either of the methods, these will be made the subject of a special discussion

An assessment was made as to whether perfusion defects with or without a ventilation defect, and a perfusion defect alone, indicated pulmonary embolism

The diagnostic specificity and diagnostic sensitivity were calculated, i e the fractions of a true pathologic and true normal result of the tests The calculations were made for the patients with confirmed or probable pulmonary embolism or those without embolism in accordance with the criteria set forth The degree of uncertainty caused by the patients without a clear diagnosis of embolism was then estimated

Statistics The Sign test was used to compare the diagnostic accuracy of perfusion scintigraphy either alone or in combination with ventilation scintigraphy Confidence limits are 95 % limits

Results

Pulmonary embolism was confirmed or considered probable in 10 patients (at autopsy in 4 at surgery in 2, and at phlebography in 4) The 2 patients in whom the diagnosis was considered confirmed at operation had had an embolectomy 10 and 14 days before the scintigraphic examinations The perfusion defects demonstrated at scintigraphy were assumed to be due to residual clots

Absence of pulmonary emboli was confirmed in 13 patients (at autopsy in 4 at surgery in 5, and by the presence of bronchial obstruction at bronchoscopy in 4) The patient with bilateral defects was included in both groups because an embolus was demonstrated in the one lung and not in the other The symptoms in the 12 patients without pulmonary emboli can be explained by the presence of other diseases malignant neoplasm of the lung in 6 instances and perforated duodenal ulcer respiratory insufficiency following pneumonectomy pneumothorax empyema following pneumonia atelectasis and malignant neoplasm in the upper mediastinum one case each, for the others

In the remaining 12 patients the presence of pulmonary embolism could not be established Phlebography could not be carried out in 5 patients because of poor condition and in 4 other patients for technical reasons In 2 patients phlebography could not be undertaken until 8 and 14 days after the symptoms of acute pulmonary embolism No thrombosis was then detected In the remaining patient thrombosis

Table 3

Calculation of diagnostic specificity assuming that all 11 patients or only 6/11 patients had pulmonary embolism

	Diagnostic specificity	
	Perfusion defects with or without ventilation defect	Isolated perfusion defect
Based on 11 cases with pulmonary embolism	$_{3}{}^{1}$ = 0 66 (0 47–0 81)	$\frac{1}{1}$ = 1 00 (0 84–1 00)
Based on 6/11 cases with pulmonary embolism	$\frac{16}{3}$ = 0 50 (0 32–0 68)	$\frac{15}{1}$ = 0 76 (0 53–0 92)

Differences significant with both calculations

pulmonary embolism on the basis of symptoms and central vein thrombosis However even if these patients are excluded from the calculations of the diagnostic accuracy of scintigraphy the conclusion remains largely the same i e that the combination of ventilation and perfusion scintigraphy has a greater diagnostic specificity than perfusion scintigraphy alone The difference is significant at the 95 % level

The evaluation of the 12 patients with uncertain diagnosis of embolism is more difficult Of these 11 had an isolated perfusion defect and one a ventilation defect in addition It is not unreasonable to assume that the ratio between scintigraphically demonstrated and actually existing emboli in these 11 patients is identical with the ratio in the group with a confirmed diagnosis i e 1 0 The clinical suggestion of pulmonary embolism was not less in these 11 patients than in the patients in whom an embolism was confirmed In addition the diagnosis was founded on ECG abnormalities suggesting an acute right sided affection (5 patients) other possible explanations of the symptoms being ruled out as well as could be anticipated on ordinary chest films in all cases and by evaluation by a cardiologist (5 patients) or physician (3 patients) Even if it is not accepted that all 11 patients had pulmonary embolism it must be considered quite improbable that at least some of them would not have had it Calculations assuming that all 11 uncertain cases or only 6 of them had pulmonary embolism appear in Table 3 The true values can be expected to lie between the two possibilities but presumably are closer to the former and consequently close to 1 0

The 12th patient with a doubtful diagnosis had symptoms and signs of embolism 14 days before examination A chest film showed nothing abnormal Both the ventilation and the perfusion scintigraphy were evenly reduced If the final diagnosis actually is embolism this case indicates that long lasting reduced perfusion affecting ventilation must be taken into consideration

However the doubtful cases be placed it appears that an isolated perfusion defect

Table 1

Diagnostic precision of perfusion scintigraphy in pulmonary embolism

Defects	Emboli		Total
	Present	Absent	
Present	10	11	21
Absent	0	2	2

Diagnostic specificity $\frac{10}{21}$ = 0.48 (confidence limit 0.26–0.70)
Diagnostic sensitivity = 1.00 (confidence limit 0.16–1.00)

Table 2

Diagnostic accuracy of ventilation perfusion scintigraphy in pulmonary embolism

	Emboli		Total
	Present	Absent	
Isolated perfusion defects	10	0	10
Combined ventilation perfusion defects (11 cases) or no defects (2 cases)	0	13	13

Diagnostic specificity $\frac{10}{10}$ = 1.00 (confidence limit 0.69–1.00)
Diagnostic sensitivity $\frac{13}{13}$ = 1.00 (confidence limit 0.75–1.00)

other 11. In Fig. 3 an isolated perfusion defect appears combined with a normal ventilation scintigraphy in a patient with pulmonary embolism.

Calculation of the diagnostic specificity and sensitivity of perfusion defects is given in Table 2 for the 23 patients with confirmed or probable presence or absence of pulmonary emboli.

Discussion

The accuracy of the pulmonary scintigraphic methods for the diagnosis of pulmonary embolism was evaluated in a series of 34 patients with possible embolism.

The presence or absence of pulmonary emboli was not possible to confirm in all the patients. Only at autopsy or surgery can a definite diagnosis be made. The combination of symptoms and thrombosis of the central veins proven at phlebography may be debatable. In the present series, 4 patients were considered to have proven

SUMMARY

In 34 patients with suggested pulmonary emboli ventilation scintigraphy with ¹ Xe and perfusion scintigraphy with Tc^m labelled albumin spheres were carried out The combined ventilation perfusion scintigraphy had a significantly higher diagnostic specificity (1 0 confidence limit 0 69–1 0) than perfusion scintigraphy alone (0 48 0 26–0 70) Both methods had a diagnostic sensitivity of 1 0

ZUSAMMENFASSUNG

Bei 34 Patienten mit vermuteter Lungenembolie wurden Perfusionsszintigraphie mit Xe und Durchstromungsszintigraphie mit Tc^m gezeichneten Albuminspharen ausgefuhrt Die kombinierte Ventilations Perfusionsszintigraphie hatte eine signifikant hohere diagnostische Spezifitat (1 0 Konfidenz Grenze 0 69–1 0) als die Perfusionsszintigraphie alleine (0 48 0 26–0 70) Beide Methoden haben eine diagnostische Empfindlichkeit von 1 0

RESUME

Chez 34 malades suspects d embolies pulmonaires une scintigraphie par ventilation avec le Xe et une scintigraphie par perfusion avec des spheres d albumine marquee par Tc^m ont éte effectuées L association de scintigraphie par ventilation et par perfusion a eu une specificité diagnostique significativement plus elevee (1 0 intervalle de confiance 0 69–1 0) que la scintigraphie par perfusion seule (0 48 0 26–0 70) Ces deux methodes ont eu une sensibilite diagnostique de 1 0

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demonstrated at combined ventilation perfusion scintigraphy has a higher diagnostic specificity than one demonstrated at perfusion scintigraphy alone The differences are significant with a 95 % limit for all the calculations made These results are consistent with those of McNEIL (1976)

KNIGHT & METREWELLI (1977) found no correlation between the presence of perfusion defects without defects also in ventilation and deep vein thrombosis as demonstrated by ^{125}I fibrinogen scanning of the legs in a postoperative series However this does not mean that such perfusion defects may not be due to pulmonary embolism since ^{125}I fibrinogen scanning is unable to detect thrombosis in the central veins in the leg above the middle of the thigh i e from the area in which pulmonary emboli originate (HAEGER & NYLANDER 1967 BRODELIUS et coll 1970 BROWSE 1972 HEDLUND 1975)

In the present series perfusion scintigraphy had a diagnostic sensitivity of 1 0 which confirms the findings of POULOSE et coll and WILLIAMS et coll (1974) Thus it would seem appropriate to carry out perfusion scintigraphy in patients with perfusion defects However this is not practical because ventilation scintigraphy cannot be carried out until several hours later after the injection of ^{99}Tc^m labelled albumin

One possibly erroneous normal result with combined ventilation perfusion scintigraphy was found, which would not have occurred if perfusion scintigraphy had been used alone

The present findings of a low diagnostic specificity for perfusion scintigraphy are in agreement with those reported by BROWSE et coll (1974) and WILLIAMS et coll as well as in one report in which as in the present series only well defined segmentally located perfusion defects were considered (POULOSE et coll)

The ability to diagnose the presence of pulmonary emboli with accuracy is particularly important because of the current interest in establishing prophylactic methods against post operative embolism Pulmonary angiography is the direct method but it is a more difficult and laborious examination Furthermore it involves a certain amount of discomfort to the patient compared with scintigraphy and it may also give ambiguous results (POULOSE et coll) Thus it would seem important to try to improve the scintigraphic methods available

Perfusion defects caused by obstruction of the pulmonary artery can be distinguished from defects secondary to reduced ventilation of a lung segment using combined perfusion ventilation scintigraphy (WILLIAMS et coll) The present results agree with their findings In evaluation of the effects of prophylactic measures against pulmonary embolism the use of combined perfusion ventilation scintigraphy is preferable to perfusion scintigraphy alone which cannot be considered sufficiently accurate

The present results show that the patients do not necessarily have to hold their breath during the examination This means that scintigraphy can be used also in patients who are in poor condition i e in whom a definite diagnosis is particularly important

FROM THE DEPARTMENTS OF SURGERY AND DIAGNOSTIC RADIOLOGY ARHUS MUNICIPAL HOSPITAL DK 8000 ÅRHUS DENMARK

POSTOPERATIVE DEEP VEIN THROMBOSIS OF THE LOWER LIMB AND PROPHYLACTIC VALUE OF HEPARIN EVALUATED BY PHLEBOGRAPHY

J KIIL and J C MØLLER

Scanning with ^{125}I fibrinogen (HUME et coll 1973 HEDLUND 1975) has demonstrated a high incidence of thrombosis of the lower limb following surgery

The prophylactic effect of low dose heparin on this disease has been demonstrated by KAKKAR et coll (1972) MACINTYRE et coll (1974) and STRAND et coll (1975) but others have been unable to achieve similar results (HAMPSON et coll 1974 COVEY et coll 1975)

Thrombosis in the central veins of the leg proximal to the midpoint of the thigh cannot be demonstrated with ^{125}I fibrinogen scanning (BROWSE 1972 COUCH 1972 MAVOR et coll 1972 HEDLUND) Thrombi at this particular site lead to pulmonary embolism (SEVITT & GALLAGHER 1961 LE QUESNE 1974) The best method for examining this region is phlebography (LE QUESNE HEDLUND KIIL & MØLLER 1979)

The incidence of thrombosis following surgery as demonstrated at phlebography and the relative frequency of thrombi likely to result in embolism was the object of the present investigation as well as the question whether the formation of the most dangerous thrombi could be prevented by low dose heparin

Material and Methods

The present report is part of a larger clinical investigation on the prophylactic effect of low dose heparin on pulmonary embolism presenting with symptoms or

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Table 1

Sites of operation in the heparin and placebo groups

	Heparin	Placebo
Stomach duodenum	2	2
Bile ducts pancreas	4	4
Colon rectum	4	4
Kidney ureters	2	3
Bladder prostate	1	5
Intrathoracic operations	5	4
Lower limbs	6	4
Total	24	26

signs, and deep vein thrombosis (KIIL et coll 1978) The material consisted of patients aged 40 years and over who were admitted for elective surgery under general anaesthesia and in whom the operation was expected to last a minimum of one hour Patients with hepatic disease or with a possible abnormal bleeding tendency were excluded Previous thrombo embolic episodes or a possible predisposition to these conditions were not regarded as criteria for exclusion

The patients were randomly assigned to one of two groups In one group the patients were given sodium heparin 5 000 units in 1 0 ml subcutaneously into the anterior abdominal wall or thigh twice daily from the evening before the operation up to and including the 7th postoperative day The other group was given 1 0 ml NaCl 0 9 per cent during a corresponding period

Care was taken that the patients included were representative of the total number in the prospective double blind trial

Fifty patients were included none having signs of deep vein thrombosis or pulmonary embolism The heparin group comprised 24 patients 13 women and 11 men with a median age of 71 years (range 43 to 84 years) The placebo group included 26 patients 12 women and 14 men with a median age of 62 years (range 41 to 89 years) Eight of the 24 patients in the heparin group and 11 of the 26 in the placebo group were operated upon for a malignant disease The sides of operation appear in Table 1

At the preoperative clinical examination varices were demonstrated in 2 patients in the heparin group One patient in each group had a past history of phlebitis Before phlebography, all patients were assessed clinically, and the diagnostic criteria used for deep vein thrombosis are described elsewhere (KIIL & MOLLER)

Phlebography Ascending phlebography was performed on the 5th to 7th post operative days i e while the patient was still receiving either heparin or placebo The technique of the phlebographic procedure and the consideration of its results have been described previously (KIIL & MOLLER)

Table 2

Results of postoperative phlebography in the heparin and placebo groups

	Heparin	Placebo	Total
Thrombosis	4	6	10
Calf veins	2	1	3
Femoral veins	2	3	5
Calf and femoral veins	0	2	2
No thrombosis	20	20	40

Based on the assumption that thrombi of a length of more than about 3 cm might cause a severe pulmonary embolism the thrombi were classified as small (<3 cm in length) or large (≥3 cm in length

Results

Postoperative phlebography demonstrated the presence of a thrombus in 10 of the 50 cases (Table 2) No patient had thrombosis of the iliac veins

The thrombi in the femoral vein were classified as large in one patient in each group and as small in one patient receiving heparin and in 4 patients receiving placebo

Thus a definite thrombus was demonstrated in 4 of 24 patients (17 per cent) in the heparin group and 6 of 26 patients (23 per cent) in the placebo group The difference is not significant

Of the 10 patients with demonstrated thrombosis symptoms of deep vein thrombosis were marked in one patient mild in 2 and absent in 7

Side effects At the beginning one patient developed a superficial phlebitis of the vein into which the contrast medium had been injected and 3 patients had swelling and soreness of the leg up to one week *after the phelebography* Therefore the technique was modified After the injection of the contrast medium the veins were flushed with physiologic saline After this modification no side effects occurred in th remaining 32 patients

Discussion

The assessment of the incidence of postoperative deep vein thrombosis of the le usually has been based on scanning after intravenous injection of ¹²⁵I labelled fibrinogen (Hobbs 1961 Atkins & Hawkins 1965) Using this method it has been shown that thrombosis occurs in about 30 per cent of patients over 40 following elective surgery lasting at least 1 hour (Hume et coll Hedlund) The diagnostic accuracy of this method has been compared to phlebography which is considered the most accurate method for demonstrating deep vein thrombosis (Rabinov &

PAULIN 1972 WILLIAMS 1973 HARRIS et coll 1974 LE QUESNE) In most reports the number of false abnormal findings with ^{125}I fibrinogen scanning is about 10 to 20 per cent (NEGUS et coll 1968 LAMBIE et coll 1970 BECKER & SCHAMPI 1973) and the number of false normals approximately 10 per cent Thus the method has a relatively high diagnostic accuracy However, the thrombi detected with this method are all located below the middle of the thigh the method having been found inaccurate at a higher level (BROWSE, COUCH MAVOR et coll , HEDLUND) Furthermore the majority of thrombi demonstrated by this method are located to the sinusoids, particularly in the soleus muscle and their clinical importance is debatable (NEGUS et coll COUCH HEDLUND) Pulmonary emboli usually tend to originate from thrombi forming in or proximal to the femoral vein and these thrombi may develop without any connection with thrombi in the legs (SEVITT & GALLAGHER LE QUESNE)

The total incidence of thrombi demonstrable at phlebography in all sections of the veins of the lower limb was evaluated in the present material as well as the frequency of those thrombi which are considered to involve a special risk of embolism The omission of a tourniquet at the phlebography is particularly important because this device prevents satisfactory filling particularly of the muscular veins

The total incidence of thrombosis in the present series was 11/50 i e 22 per cent (in the heparin group 17 and in the placebo group 23 per cent) which is somewhat lower than what is usually obtained with ^{125}I fibrinogen scanning This suggests that ^{125}I fibrinogen scanning overestimates the frequency of thrombosis Also the distribution of thrombi between major and peripheral veins as demonstrated by phlebography and the fact that ^{125}I fibrinogen scanning cannot detect thrombi in the central femoral or pelvic veins indicates that the fibrinogen method is unsuitable for assessing the incidence of thrombi likely to cause embolism

The present information does not allow any conclusion as to the effect of low dose heparin on the formation of phlebographically demonstrable or clinically important thrombi The frequency of these thrombi is so low that a much more extensive series would be needed

SUMMARY

The incidence of postoperative thrombosis of the leg at phlebography and the prophylactic effect of low dose heparin was assessed in a double blind investigation comprising 50 patients Thrombosis occurred in 17 per cent in the heparin group and in 23 per cent in the placebo group This difference is not significant No prophylactic effect of low dose heparin was demonstrated

ZUSAMMENFASSUNG

Das Vorkommen einer postoperativen Thrombose des Beins bei der Phlebographie und der prophylaktische Effekt einer niedrigen Dosis von Heparin wurden in einer Doppelt Blind Untersuchung die 50 Patienten umfasste festgestellt Eine Thrombose trat in 17

Prozent bei der Heparingruppe und in 23 Prozent bei der Placebogruppe auf Der Unterschied ist nicht signifikant Kein prophylaktischer Effekt wurde mit Heparin in niedriger Dosis nachgewiesen

RESUME

La frequence de la thrombose post-opératoire du membre inferieur après la phlebographie et l effet prophylactique d une faible dose d heparine ont eté etudiés dans une recherche en double insu comprenant 50 malades La thrombo e s est produite dans 17 pour-cent des cas traites par l heparine et dans 23 pour cent du groupe traite par un placébo Cette difference n est pas significative Les auteurs n ont pas mis en evidence un effet prophylactique d une faible dose d heparine

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FROM THE DEPARTMENT OF DIAGNOSTIC RADIOLOGY RIKSHOSPITALET OSLO NORWAY

VENOUS STRUCTURES OF THE CHEST AND ABDOMEN AT COMPUTER TOMOGRAPHY

A KOLBENSTVEDT F KOLMANNSKOG and T AAKHUS

With the introduction of computer tomography (CT) in clinical practice a review is needed of the anatomy of transverse sections of the body Vascular structures are present in every section Some of these are easily recognized but when anomalous or abnormally dilated vessels are present these may cause difficulties in the analysis of the ima es The purpose of the present report is to describe the appearances of some normal and abnormal venous structures as demonstrated at computer tomography of the thoracic and abdominal regions

A Delta Scan 50 FS with a scan time of 18 s and a 256 × 256 matrix display was employed At each scan two cross sectional reconstructions were obtained each re presenting a tissue thickness of 13 mm The patients were asked to hold the breath during the canning The CT examination was monitored by an experienced radio logist Contrast medium was given intravenously or orally and anticholinergic agents used whenever considered necessary

During the period from September 1977 to September 1978 1 238 examinations were performed of the abdomen and 322 of the thorax The illustrations of the present report are selected from this material

The frequency with which vascular structures appear in clinical series depend on a

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Fig. 3 a) Widened azygos vein in a patient with thrombosis of the inferior vena cava appears as a round structure (arrow) in the posterior part of the mediastinum to the right of the descending aorta b) Section immediately above bifurcation of trachea The vein (arrow) points forwards and to the right c) Adjacent cranial section The vein (arrow) arches to the right of the trachea towards the superior vena cava

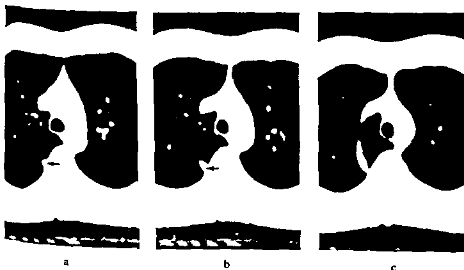


Fig 4 a) Section through lower part of aortic arch Anomalous azygos vein (arrow) appears like a small nodule to the right of the spine and may simulate a subpleural metastasis b) Adjacent cranial section The vein (arrow) is more prominent and points in a forward and lateral direction c) Further cranial section The vein arches towards the superior vena cava Chest film disclosed an azygos lobe of the lung



Fig 1

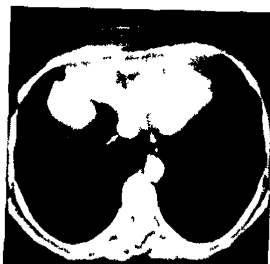


Fig 2

Fig 1 Section through the aortic arch Superior vena cava (arrow) is clearly distinguished

Fig 2 Section through the upper pole of the right diaphragm Inferior vena cava (arrow) appears as a bulge on the posterior aspect of the heart

number of factors such as the technical quality of the scanner thickness of the sections and distance between sections use of anticholinergic drugs and intravenous contrast medium The general condition and the weight of the patient play also an important role more details are discernible in obese patients without dyspnoea Due to the variability of many of these parameters in the present series a quantitative analysis has not been performed

Veins of thoracic region

The superior (Fig 1) and the inferior vena cava were the most prominent veins above the diaphragm The former was situated anterior and to the right of the trachea and to the right of the ascending aorta Its visibility depended on the degree of distension and the amount of mediastinal fat separating it from the aorta or from pathologic conditions such as mediastinal or pulmonary expanding lesions Using a *Delta Scan* 50 with a scan time of 2 min and 43 s GOLDWIN et coll (1977) found that the superior vena cava was demonstrated in all of 84 examined patients

The pulmonary *veins were discernible behind the heart but were of no diagnostic* importance in the present series Patients with pulmonary congestion as a rule could not hold the breath satisfactorily the degree of filling and distension of the pulmonary *veins were* better evaluated on conventional chest films

The short thoracic part of the inferior vena cava (Fig 2) was usually less evident than the superior vena cava because of the adjacent heart or diaphragm but it was



Fig 3 a) Widened azygos vein in a patient with thrombosis of the inferior vena cava appears as a round structure (arrow) in the posterior part of the mediastinum to the right of the descending aorta b) Section immediately above bifurcation of trachea The vein (arrow) points forwards and to the right. c) Adjacent cranial section The vein (arrow) arches to the right of the trachea towards the superior vena cava



Fig. 4 a) Section through lower part of aortic arch Anomalous azygos vein (arrow) appears like a small nodule to the right of the spine and may simulate a subpleural metastasis b) Adjacent cranial section The vein (arrow) is more prominent and points in a forward and lateral direction c) Further cranial section The vein arches towards the superior vena cava. Chest film disclosed an azygos lobe of the lung



Fig. 5. a) Section below the kidneys. The shape of inferior vena cava (arrow) is oval with right margin more posterior than the left. b) Same section during straining after expiration. Flattening of the vein.

clearly outlined in patients with emphysema of the lungs or during a particularly deep inspiration. When visible, it had the appearance of a round bulge of the right posterior aspect of the heart.

The azygos vein was visible prevertebrally on the right side of the descending aorta behind the right diaphragmatic crus as indicated by CALLEN et coll. (1977). It could not be distinguished from the lymph nodes of that region unless seen in several adjacent sections or enhanced by contrast medium. When enlarged, e.g. in a case with obstruction of the inferior vena cava, the azygos vein simulated a posterior mediastinal mass (Fig. 3 a). The true nature of the structure was revealed by analysing adjacent sections up to the point where the vein arched over the right main bronchus (Fig. 3 b, c) and emptied into the superior vena cava. At this level, the distance between the tracheal lumen and the right lung was larger than in the more cranial sections. In patients with an azygos lobe of the lung, the azygos vein ran a more lateral course and arched forwards at a more cranial level than usual. The air filled azygos lobe was located between the arch of the vein and the mediastinum (Fig. 4). In sections immediately above the tracheal bifurcation the anomalous azygos vein simulated a subpleural metastasis situated to the right of the spine (KOLBENSTVEDT et coll., in press).

Veins of abdominal region

The inferior vena cava was the most prominent infradiaphragmatic vein being visible in most abdominal sections. Its cross sectional shape was oval and obliquely oriented with the right margin more posterior than the left (Fig. 5). This fact explains why the right margin of the vein is often better delineated than the left at cavography in supine position due to layering of the contrast medium (GABRIELE et coll. 1967). In some patients the vein was surprisingly flat with the shortest diameter no wider than



a



b

Fig. 6 Patient with tumor of the right kidney revealed by CT a) Central dark spot in the inferior vena cava (arrow) represents a tumor thrombus b) Phlebography of inferior vena cava with thrombus

that of the renal vein (Fig 12) This might be due to an unintentional straining during the prolonged period of holding the breath The flat shape of the inferior vena cava durin intentional straining following expiration is illustrated in Fig 5 b

In a patient with a vertebral destruction abdominal CT revealed a renal tumor on the ri ht side A central zone of less attenuation in the inferior vena cava (Fig 6 a) was considered to represent a thrombus which was confirmed by phlebo graphy (Fig 6 b) Tumor extension through the right renal vein into the inferior vena cava was found at surgery A similar finding was reported by STEELE et coll (1978) They pointed out that artifacts consisting of concentric rings centered at the midpoint of the scanning field might simulate thrombosis if the center be superimposed on one of the great vessels

The hepatic segment of the inferior vena cava (Fig 7) presented as a round area of low attenuation medially in close relation to the caudate lobe Smaller similar areas of low attenuation in the vicinity represented the hepatic veins The characteristic location of such single large and multiple smaller areas as a rule made recognition easy If doubt existed as to the nature of the finding intravenous contrast medium from the foot revealed the true size of the caval lumen (Fig 7 b) On scans of patients in the left lateral decubitus position the liver was found to gravitate towards the left and pull the inferior vena cava forwards Phlebography of the vein in lateral projection should therefore not be performed in the left lateral decubitus position as the forward movement of the vein may be difficult to distinguish from displacement by a retro caval expanding lesion (LIEN personal communication)

The hepatic veins appeared as either round or oval areas of low attenuation or as linear structures of similar attenuation converging towards the inferior vena cava (Fig 8)

The branches of the portal vein ran from the hilar region into the left and right



a



b

Fig 7

Fig 7 Section through the liver of a 20 year old woman previously operated for tumor of the pancreas a) Hepatic segment of the inferior vena cava (large arrow) appears as a round area of low attenuation which should not be considered as metastasis Small arrow indicates hepatic vein b) Same section after injection of contrast medium in a vein of the foot



Fig 8 Section through the liver indicating a left a middle and a right hepatic vein converging towards the inferior vena cava (arrow)

Fig 8

liver lobes (Fig 9 a) Following intravenous injection of vascular contrast medium the portal veins became indistinguishable (Fig 9 b) while dilated bile ducts remained visible as indicated by KRESSEL et coll (1977) In patients with fatty liver the vessels were clearly outlined due to the low attenuation of the hepatic parenchyma (Fig 10)

CT examination of a patient with portal hypertension revealed a round structure along the caudal part of the anterior surface of the liver (Fig 11) with attenuation values close to those of the inferior vena cava before and after intravenous contrast medium The structure was also observed in the midline above the umbilicus Angiography of the coeliac trunk confirmed the suggestion of hepatofugal flow through a dilated umbilical vein

The left renal vein appeared as a linear structure which crossed the midline between the aorta and the superior mesenteric artery (Fig 12) and joined the inferior vena cava posterior to the pancreatic head *KUHNS et coll (1978) reported this junction to be a* useful guide in localising the head of the pancreas which was found anterior to the





a Fig 9 b



Fig 10

Fig 9 a) Section through the liver Linear branching structures (arrows) to the right and left lobes represent portal venous branches b) Same section after intravenous injection of contrast medium The linear structures have disappeared indicating that they were venous branches and not dilated bile ducts

Fig 10 Section through the liver The attenuation value of the hepatic parenchyma was 20 Hounsfield units indicating a fatty liver Inferior vena cava and intrahepatic vessels visible as structures of higher attenuation

confluence in 16 of 17 patients In the present series one patient had a circumaortic venous ring demonstrated at angiography The retroaortic venous limb could not be clearly identified at CT

The splenic vein was found to cross the midline behind the pancreatic body anterior to the aorta and anterior or superior to the superior mesenteric artery The vein was more often visible in one section than the splenic artery because of the tortuosity of the latter The pancreatic body and the splenic vein appeared as parallel structures The fat separating them (Fig 13) occasionally simulated a dilated pancreatic duct which has also been pointed out by SEIDELMANN et coll (1977) Erroneous interpretation of similar images can be found in the literature The contours of the splenic vein were smoother than those of the more lobulated pancreas (Fig 13) Bearing this in mind the confusion with a dilated pancreatic duct should be avoided

The superior mesenteric vein and the extrahepatic portal vein were less easily distinguishable than the renal and splenic veins because of their proximity to adjacent



a



b

Fig 11 Patient with portal hypertension a) Section through lower part of the liver indicates a dilated umbilical vein (arrow) b) Portal phase of coeliac angiography The dilated umbilical vein (arrows) is clearly visible



Fig 12



Fig 13

Fig 12 Left renal vein crossing the midline behind the superior mesenteric artery (small arrow) The inferior vena cava is unusually flat Pancreatic head (P) in front of junction between renal vein and vena cava Superior mesenteric vein (large arrow) close to the head of the pancreas

Fig 13 Section through the pancreatic body and the splenic vein which crosses the midline anterior to the superior mesenteric artery The space between the pancreas and the splenic vein (arrow) may simulate a wide pancreatic duct unless the smoother outline of the vein is appreciated

organs like the head of the pancreas and because of their more cranio caudal orientation The *superior mesenteric vein could occasionally be distinguished* on the right side of the superior mesenteric artery as a bulge of the medial surface of the pancreatic head (Fig 12)

The pelvic veins were more difficult to differentiate than the inferior vena cava due to their smaller caliber the oblique orientation and the close proximity to the iliac arteries The variability in the size of the psoas muscles and the surrounding pelvic lymph nodes further contributed to these difficulties In the present series no indication was found for contrast medium enhancement of the pelvic veins

Comments The increasing importance of whole body computer tomography in clinical radiology necessitates a thorough knowledge of the anatomy of transverse sections vascular structures included

Although angiography reveals more details much information can be obtained at CT about pathologic conditions such as thrombi or abnormal dilatation The vessels may serve as a useful guide in localising organs and anomalous or abnormal veins may simulate pathologic conditions

SUMMARY

From a total of 1 560 CT examinations of the thorax and abdomen transverse sections illustrating various normal and abnormal venous structures were selected The radiologic importance of these structures is pointed out

ZUSAMMENFASSUNG

Von 1 560 CT Untersuchungen des Thorax und Abdomens wurden Querschnitte die verschiedene normale und pathologische Venen Strukturen darstellen ausgewahlt Die rontgenologische Bedeutung dieser Strukturen wird hervorgehoben

RÉSUMÉ

Sur un total de 1 560 examens tomodensitometriques du thorax et de l abdomen les auteurs ont choisi des coupes axiales illustrant diverses structures veineuses normales et anormales Ils soulignent l importance radiologique de ces structures

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FROM THE DEPARTMENTS OF EXPERIMENTAL RESEARCH PATHOLOGY AND DIAGNOSTIC RADIOLOGY MALMO ALLMANNA SJUHHUS S 21401 MALMO SWEDEN

COLON OF THE RAT

An anatomic histologic and radiographic investigation

C G LINDSTRÖM J E ROSENGREN and F T FORK

The anatomy of the colon of the rat has been described previously but even in recent works errors and misinterpretations may be found (SPJUT & SPRATT 1965 SMITH & CALHOUN 1968 WARD 1974)

Attempts have also been made to apply the terminology of human anatomy to the rat colon (MARTIN 1923 NORDBERG 1946 ROWETT 1952 GREEN 1955 CHIASSON 1969 POZHARISSKI 1973) which from a topographic and radiographic point of view is confusing The colon anatomy of the rat differ greatly in essential features from that of man both macro- and microscopically Knowledge of the normal anatomy is a prerequisite for understanding and evaluation of morbid conditions both patho- lo ically and radiographically

Material and Method

Radiologic examinations necropsies and pathologic examinations of 300 carcinogen treated white Wistar/Furth rats supplemented by an investigation of 40 normal animals of varying age (2 weeks—adults) formed the basis of this report All the rats had been raised on a diet of pellets and water ad libitum The colon of 20 normal adult animals were radiographically examined

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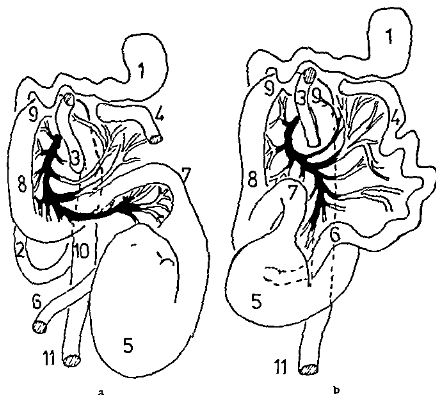


Fig. 2 Schematic drawings with the caecum a) to the left and b) to the right Position of the common mesentery 1) stomach 2) descending duodenum 3) ascending duodenum 4) small intestine 5) caecum 6) distal ileum 7) small flexure of the proximal colon 8) proximal colon 9) major flexure 10) distal colon 11) rectum (cut)

The colon including caecum and rectum is in the adult white rat about 21 to 27 cm in length The caecum is 5 to 7 cm in length and considerably wider than the other parts of the colon It is slightly kidney formed with a concave minor curvature in which the distal ileum ends close to the opening for the proximal colon and a convex major curvature (Figs 1 2) The caecum has no appendix

The proximal colon 5 5 to 6 5 cm in length has a marked oblique folding of the mucous membrane with a palm leaf appearance (Fig 3 a) The proximal colon passes over into a major flexure 3 to 3 5 cm in length which describes a cranio-convex bend around the mesenteric root The characteristic appearance of the mucous membrane in the proximal colon changes in the major flexure as a transitional zone with a usually more protuberant mucous membrane into longitudinal folds These are typical of the distal part of the colon 4 5 to 6 5 cm in length and the rectum 3 to 3 5 cm in length (Fig 3 a)

Haustra and taenia are absent in the colon of the rat



Fig 1 The rat colon in situ The ventral abdominal wall removed Caecum to the left Relation of major flexure to the stomach and duodenal loop

Barium enemas were performed in 2 normal rats and double contrast technique (ROSENGREN 1978) was used in the remaining 18 The barium enema examinations were carried out with an inflated balloon in the rectum The colon was filled with 15 to 20 ml barium contrast Fluoroscopic control was used in order to avoid distension of the organ and passage of contrast medium into the distal ileum The animals were subjected to necropsy and pathologic examination

After inspection of the abdominal organs in situ the colon was resected slit up, mounted on a wooden plate with pins and fixed in buffered 10 per cent formalin The colon specimen was then photographed and notations were made of macroscopically observed structures such as length of different parts appearance of the mucous membrane localization of lymphoid patches etc

Sections were made from different parts of the colon for microscopy Staining with hematoxylin eosin was used as the basic method which in selected cases was combined with mucus stains, McManus (PAS) and alcian blue (pH 2 5)

Results

Gross morphology The large bowel in the rat can be divided into 5 main parts caecum proximal colon major flexure distal colon and rectum

The rat colon has a well developed lymphoid apparatus with lymphoid plaques (Fig 3) They are fairly regularly distributed within certain regions of the rat colon Thus plaques are found in 4 distinct areas the caecum about 4 5 mm × 3 mm in size the proximal colon about 45 mm from the junction caecum proximal colon about 4 5 mm × 3 5 mm in size the distal part of the major flexure about 4 5 mm × 3 mm in size and the distal colon at the borderline to rectum about 8 5 mm × 4 0 mm in size (Fig 3 b) on an average of 32 5 mm above the anus

Furthermore lymphoid plaques may occur in somewhat varying positions in the middle part of the caecum about 3 5 mm × 2 5 mm in size and in the distal colon about 3 5 mm × 2 mm in size

Topographic anatomy The caecum is the widest part of the colon (Fig 1) Together with the proximal colon and the small intestine except for the duodenum it has a common mesenterium with a slender fixation to the dorsal wall of the abdomen Consequently the caecum and proximal colon are mobile and may have different positions in the abdominal cavity with the caecum often situated to the left (Figs 1 10) From the caecum the proximal colon runs to the right hypochondrium in a spiral formed course with a smaller flexure after the passage from the caecum (Fig 4)

Close to the right part of the liver the proximal colon continues in a cranio-convex major flexure This surrounds the mesenteric root from the right to the left The major flexure lies ventro medial to the descending duodenum bordering dorsad on the duodenal mesentery craniad and ventrad on different parts of the liver and also craniad on the duodenal bulb and parts of the stomach (Figs 1 2) The flexure is ventrally superimposed by or situated cranial to the duodeno jejunal junction The major flexure passes over into the distal colon ventral to the mesenteric root including the large abdominal vessels and with the ascending duodenum to the right The distal colon follows a descending course in the median line attached to the dorsal abdominal wall by a short mesentery with vessels to the bowel wall Just before the entrance to the lesser pelvis the distal colon borders ventrally on the urinary bladder In the pelvic cavity the rectum lies in the midline dorsal to the urethra and ventral to the sacrum The rectum has a short mesenteric fixation of the type observed in the rest of the distal colon and is loosely attached by connective tissue to the surroundings The proximal part of the rectum which passes the bony pelvis is somewhat narrower than the distal colon and the distal rectum (Figs 1 3 a)

The mesenteric root with the superior mesenteric artery is fixed in the midline and the attachment of the distal mesocolon extends along the vertebral column From the mesenteric root the common mesentery spreads out fan shaped supplying the small intestines caecum and proximal colon

Histology The colonic and rectal mucosa consists of a lamina propria with tubular glands lined by cylindric epithelium (of absorptive type) and goblet cells (Fig 5) The glandular architecture varies in the different parts of the colon



Fig 3 a

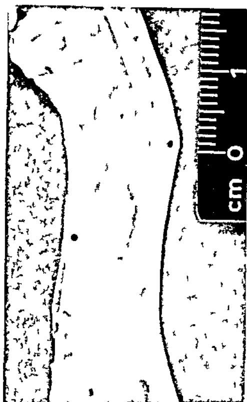


Fig 3 b

Fig 3 a) Rat colon after having been mounted and fixed on a wooden plate Typical palm leaf ap pearance of the proximal colon and longitudinal folds of the distal colon and rectum Lymphoid plaques (→) b) Photograph of a lymphoid plaque in the distal colon with small indentations



Fig 4 Right oblique view of the caecum proximal colon and major flexure of a rat colon in situ

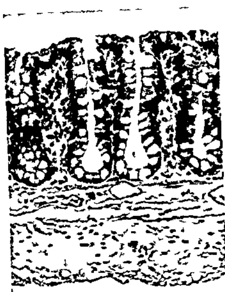


Fig 5



Fig. 6

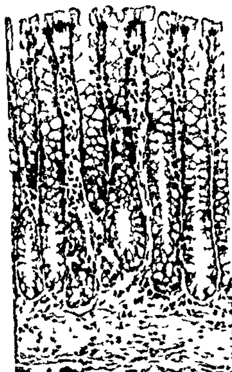


Fig 7

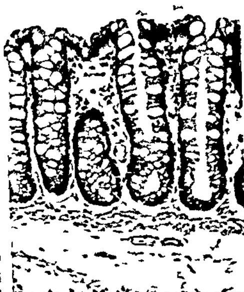


Fig 8

In the caecum mucosal glands of the tubular type are lined by cylindric epithelial cells and goblet cells The goblet cells are rather evenly distributed in the various parts of the tubules yet somewhat more marked in the basal parts of the tubular crypts (Fig 5)

In the proximal colon the tubular glands are somewhat branched basally and in the basal parts of the tubular glands there is a marked occurrence of rather large pale, goblet like cells These have staining properties differing from the usual goblet cells with only faint or no PAS reaction (Fig 6) This type of cells seems to be characteristic of the proximal colon

In the major flexure the mucosa is thicker than in the other parts of the colon and rectum (Fig 7) The tubular glands are longer The epithelial lining of the tubular crypts has properties of both the proximal and distal colonic mucosal types It could be looked upon as a transitional zone with successively diminishing number of the characteristic cells in the basal crypts of the proximal colon

The mucosa in the distal colon is thinner than the mucosa in the major flexure (Fig 8) The tubular glands are lined by epithelium with rather small goblet cells in the basal parts of the tubular glands as compared with the upper parts

There is no considerable difference in the epithelial lining of the tubular glands in the rectum as compared with that of the distal colon Especially in old rats the glands are often somewhat more loosely arranged near the anorectal margin

In the various parts of the colon the epithelial regeneration seems to occur in the lower two thirds of the tubular glands where mitoses are most frequent

Basally in the mucosa there is a thin layer of muscularis mucosae with an inner part of circularly arranged smooth muscle cells and an outer part of obliquely or longitudinally arranged muscle cells Outside the muscularis mucosae is the submucosa with connective tissue containing vessels and scattered nerve ganglion structures

The external tunica muscularis (muscularis propria) lying outside the submucosa consists of an inner thicker part of mainly circularly arranged smooth muscle cells and an outer (external) thin layer of mainly longitudinally arranged muscle cells No evident taenia structures exist in the colon Between the 2 parts of the muscularis externa there are ganglion cells (plexus myentericus)

Fig 5 Caecum Evenly distributed goblet cells in the glandular crypts somewhat more marked in the crypt bases Htx E × 169

Fig 6 Proximal colon Typical appearance with numerous rather large pale goblet like cells in the crypt bases Htx E × 169

Fig 7 Major flexure Transitional zone with changing character of the mucosa The mucous membrane is higher than in the other parts of the large bowel The glands are lined with epithelium that has some characteristics of both proximal and distal colon Htx E × 169

Fig 8 Distal colon The occurrence of goblet cells is somewhat more marked in the upper parts of the glandular crypts This type of mucosa is also present in the rectum Htx E × 169


a


b

Fig 12 Rat examined a) with barium enema and b) with double contrast examination Caecum is to the right

The regions where the lymph follicles perforate the muscularis mucosae are marked macro and microscopically by small indentations in the mucosa These appear as spots of contrast medium at radiography (Fig 14)

Radiology In the a p projection the major flexure i situated with few exceptions in the right hypochondrium This gives a simple orientation in examination of films of rat colon (Fig 10)

As the rectum is fixed the description of the radiologic appearance of the rat colon is made in aboral oral direction The rectum is located centrally in the lesser pelvis and extends in close connection to the sacrum from the anus to the level of S3 while the colon leaves the lesser pelvis In the lateral view the distal colon runs straight orally to the upper abdomen (Fig 11) In a p projection the distal colon runs via a gentle arc into the major flexure

In the a p projection and with barium enema technique without distention of the colon the major flexure is almost semicircular and has its center in the right hypo chondrium (Fig 12) In the major flexure regularly a kink in the mesenteric border of the colonic wall causes an impression into the lumen

With distention by air insufflation of the colon the major flexure rises from its ordinary position and the semicircular form assumes a more paraboloid form At the same time the vertex of the flexure is displaced medially and the kinking of the mesenteric border of the colonic wall becomes more evident (Fig 12)

The proximal colon has a varying course depending on the position of the caecum (Fig 10) Several alternatives are possible (Fig 13) The oral part of the proximal colon close to the caecum forms a flexure the minor flexure The mucous membrane of the proximal colon has a peculiar palm leaf appearance which always is evident



Fig 9 Lymphoid plaque Small indentations in the mucosa corresponding to the openings in the muscularis mucosae Htx E × 37



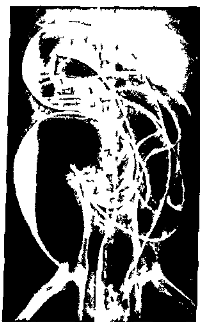


Fig 10

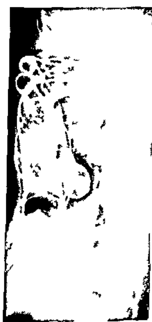


Fig 11

Fig 10 The same rat examined on 2 occasions with double contrast technique A p view Different positions of caecum and proximal colon

Fig 11 Double contrast examination of a rat in right lateral position

Outside the external muscularis is the serosa with mesothelial cells of the peritoneum Between the muscularis propria and the serosa is a subserosa of varying appearance with fat and connective tissue

The lymphoid plaques (Fig 3) are collections of lymph follicles in the boundary between the mucosa and submucosa perforating the muscularis mucosae (Fig 9)



Fig. 14 Typical radiographic appearances of lymphoid plaques in a) a p and b) lateral view

The mucous membrane especially in the distal part has many similarities to that in man On the other hand the tubular glands in the mucous membrane of the proximal colon have a characteristic appearance which distinguishes them from the glands within other parts of the colon (WARD) In the crypt bases of the glands there is an abundance of rather large pale goblet like cells with histochemical characteristics with faint or no PAS reaction (MARTIN 1961) differing them from ordinary goblet cells This type of cells in the proximal colon may be a special type of epithelium because of their staining properties (FILIPE 1975)

Injections of carcinogenic agents yield in the proximal colon a high frequency of poorly differentiated mucus producing adenocarcinomas usually of signet ring cell type This is a type of malignancy rather seldom seen in the colon and the rectum in man (WARD LINDSTRÖM et coll 1978) The tumours in the distal colon and rectum of the rat are microscopically similar to those in man

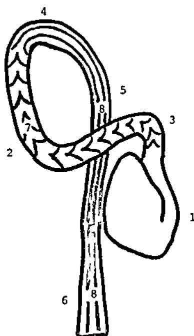


Fig 15 Proposed anatomic nomenclature of the colon of the rat Colon mobile 1) caecum 2) colon proximale pars proximalis coli 3) flexura minor coli 4) flexura major coli Colon fixum 5) colon distale pars distalis coli 6) rectum 7) plicae palmatae 8) plicae longitudinales

Within the distal part of the colon a longitudinal folding of the mucous membrane is macroscopically visible In this part the glands are coated with epithelium con taining goblet cells which are larger in size in the upper parts of the glandular crypts The rectum is not distinctly delimited from the distal colon as far as the mucous membrane is concerned and does not have any observable transversal folds of the mucous membrane as has been described by some authors (SMITH & CALHOUN WARD)

The mucosal appearance in the various parts of the colon seems to be so charac teristic that it may help in histologic localization of lesions in the colonic mucosa Lymphoid plaques are normal structures and are thus not a result of treatment with carcinogens, which has been suggested by some authors (SPJUT & SPRATT) nor should they be considered precancerous (SPRINGER et coll 1970 ROGERS et coll 1973)

The radiographic appearance of the normal colon of the rat has hitherto not been described The barium enema technique well reflects the normal anatomy and topo graphy of the colon but is not sufficient for detailed analysis of the colonic mucosal structure With the double contrast technique the colon rises and widens In the proximal colon it is always possible to detect the typical mucous membrane ap pearance and in general to observe small accumulations of contrast spots representing lymphoid plaques These structures are identified with acceptable certainty only with the double contrast technique (ROSENGREN & LINDSTRÖM 1978)

The results of the present investigations have clearly demonstrated a need of an appropriate *anatomic nomenclature of the colon of the rat* Without any prerogative the authors propose the nomenclature presented in Fig 15 to be used in the future

SUMMARY

The anatomy and radiologic appearance of the colon in rats are described on the basis of 300 animals treated with carcinogenic agents and 40 normal rats The macroscopic and microscopic appearance of the mucosa varies in the different parts of the colon Lymphoid plaques are normal structures The results justify a new anatomic nomenclature

ZUSAMMENFASSUNG

Das anatomische und rontgenologische Bild des Ratten Kolons wurde auf der Basis von 300 Tieren die mit karzinogenen Substanzen behandelt worden waren und 40 normalen Ratten beschrieben Das makro- und mikroskopische Bild der Mucosa unterscheidet sich in verschiedenen Teilen des Kolons Lymphoide Plaques sind normale Strukturen Die Ergebnisse rechtfertigen eine neue anatomische Nomenklatur

RESUMÉ

L anatomie et l aspect radiologique du colon du rat sont decrits à partir de 300 animaux traites par des agents carcinogenes et a partir de 40 rats normaux L aspect macroscopique et microscopique de la muqueuse est different dans les differentes parties du colon Les plaques lymphoides sont des structures normales Ces résultats justifient une nouvelle nomenclature anatomique

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PROTOTYPE IONOGRAPHIC IMAGING CHAMBER

Construction and clinical use

W W SEELENTAG and J W BOAG

Xeroradiography exploits the photoconductivity of selenium to record the cross sectional intensity distribution of a roentgen ray beam as a pattern of electric charge A latent image of the object is formed in this way and is subsequently made visible by powder development (DESSAUER & CLARK 1965 BOAG 1973) This technique is now well established for mammary radiography (WOLFE 1972) and for some other special radiographic procedures An alternative method of forming a latent image by col lecting the ions created by roentgen rays in a gas filled ionization chamber was first demonstrated by THOMPSON (1896) and almost simultaneously though published later by RIGHI (1903) The ions created in air by radiation having passed through an object were collected on an insulating plate and the resulting charge patterns were developed with electroscope powder—a mixture of powdered sulphur and red oxide of lead which when shaken up gave an aerosol of positively charged lead oxide particles and negatively charged yellow sulphur particles—a two tone image In principle this is identical with modern xerographic development However neither THOMPSON nor RIGHI succeeded in producing highly resolved images and no further work on the method appears to have been made for many years

REISS (1965) revived the idea improving resolution by using very small gap widths and increasing sensitivity by electron avalanche amplification An imaging chamber based on the ideas of REISS was later built at this Institute (JOHNS et coll 1975)

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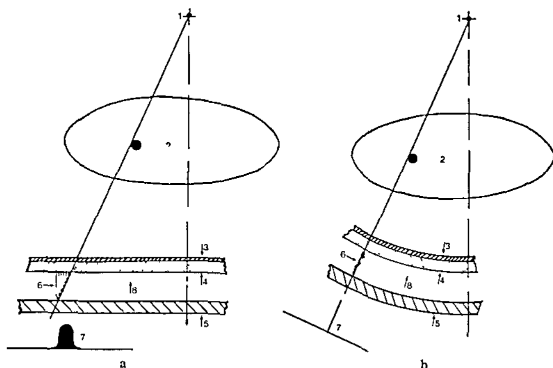


Fig 1 Eliminating off axis blurring by adopting spherical geometry 1 = radiation target 2 = absorbing object 3 = conducting layer 4 = insulting foil 5 = lower electrode 6 = ion paths during charge collection 7 = charge image of a particular photon path 8 = electric field direction

A characteristic feature of all the images produced with this chamber was their mottled appearance Detailed analysis of the results revealed that this was due to the *noise associated with high avalanche amplification* (BOAG et coll 1974) *In order to* achieve acceptable sensitivity without avalanche amplification a system with much higher quantum absorption efficiency has to be used e g an ionization chamber with a wide gap, filled with a gas of high atomic number at high pressure This principle is called ionography

An equipment employing the same principle has been developed simultaneously in the U S A by the firm of Xonics Inc (PROUDIAN et coll 1974) and some clinical images have been published both by Xonics and by the radiologic team at Hahnemann Hospital, Philadelphia *using the first prototype equipment built by Xonics* (STANTON et coll 1973 1975) This system is called electron radiography

Design of an ionographic imaging chamber

An ionography chamber consists of a large area ionization chamber with electrodes spaced some 1 to 4 cm apart The radiation transmitted through the object traverses the chamber normally creating mainly photoelectrons in the gas and these in turn form many more ions along their tracks If the range of photoelectrons is short the ionization intensity at a given point in the gas can be taken to be proportional to the intensity of the transmitted beam of photons at that point The ions and electrons

Table 1

Tolerable errors in the positional parameters of an ionography chamber (30 cm diameter 100 cm FFD) in order to preserve a resolution of 10 line pairs/mm

Parameter	FFD D = 100 cm	Eccentricity ε	Angle of tilt α	Foil centre displacement δ
Tolerable error	±5 cm	±0 7 cm	±0 4	±0 1 cm

formed are propelled across the gas space by a high potential maintained between the electrodes If one electrode is covered with a layer of insulating material the ions reaching it will accumulate on the surface to form charge variations representing the intensity distribution of the roentgen rays entering the chamber

At first sight it seems impossible to achieve good spatial resolution with widely spaced electrodes because at off axis points in any plane parallel chamber the photons traverse the gap obliquely and ions produced by successive photons traversing the same path would be collected over a wide area (Fig 1 a) Any sharp spatial discontinuities in the radiation intensity would therefore be blurred in the charge distribution this blurring increasing with distance from the axis In the imaging chamber this difficulty is avoided by using spherically curved electrodes (U S Patent No 3 963 924 and others applied for British Patent No 1 471 871) whose centre of curvature coincides with the focal spot of the tube (Fig 1 b) With this arrangement the photon paths coincide with the lines of force of the ion collecting field and the obliquity problem vanishes A rigid link between the tube and the imaging chamber is needed in order to maintain this geometry accurately The errors in alignment which can be tolerated for a target to-chamber distance of 100 cm a chamber diameter of 30 cm and an electrode spacing of 1 5 cm without causing a line spread greater than 0 1 mm can be calculated by elementary geometry (Table 1) From this table it is evident that there should be no difficulty in keeping within the tolerances of target to-chamber distance and of foil curvature The correlated errors of eccentricity and tilt are the critical ones but these can be kept within the permitted limits by rigid coupling

Table 2

Sources of reduced resolution in ionography (Calculations based on a 30 cm diameter chamber 100 cm FFD with 1 cm electrode spacing filled with xenon at 1 MPa (10 atm) and exposed to 65 kV filtered through 2 mm Al)

Source of blurring	Line width
Range of photoelectrons and Auger electrons 50 of *ions produced within*	*0 35 mm*
K fluorescence photons several cm range	General background
Dispersion of ions by diffusion (for 20 kV/cm collecting field)	
for electrons	0 8 mm
for ions	0 04 mm
Obliquity of photon paths at edge of plane parallel	
chamber 30 cm across	1 5 mm
in spherical geometry	0 *mm*

between the tube and the imaging chamber This need be no disadvantage where an equipment is set aside for one special procedure as in mammary radiography though it restricts freedom for general work

Other sources of blurring which might be expected to affect a gas filled imaging chamber are on the one hand the range of the photoelectrons formed in the gas and of the associated fluorescent photons and on the other hand the lateral diffusion of the ions when crossing the gap especially in a wide gap chamber The range of the photoelectrons is reduced, of course by using moderately high pressure gas this being necessary in any case to achieve the desired high quantum absorption efficiency A detailed analysis of the physical processes involved in ion formation and collection (JOHNS et coll 1975) has shown that for roentgen rays in the normal diagnostic energy range using xenon at 1 MPa (10 atm) as an absorber and a 1 cm electrode spacing neither the range of the secondary electrons nor the lateral diffusion of the ions should prevent good resolution being preserved in the charge distribution This is confirmed by the images obtained The K fluorescent photons travel so far that the ions produced by their reabsorption do not contribute to image formation but merely raise the background charge level over the whole image When edge contrast development is adopted this increase in background level does not appear as fog in the image K fluorescence therefore causes a loss of efficiency but not of resolution or contrast

In a noble gas like xenon subjected to a strong electric field any electrons which remain free can acquire agitation energies far in excess of the thermal energies of the gas molecules and they therefore diffuse more readily Therefore if these electrons liberated in the gas are collected instead of the positive ions the image is seriously blurred (JOHNS et coll 1974) This can be prevented by mixing with the xenon a small

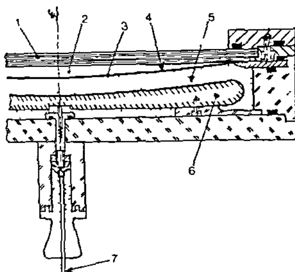


Fig 2 Half sectional view of the ionography chamber 1 = entrance window made of carbon fibre composite 2 = nitrogen 3 = Mylar foil 4 = aluminium conducting backing 5 = imaging gas (CF_3Br or Xe) 6 = lower electrode 7 = high potential lead

proportion of electron affinic gas to capture the free electrons and form negative ions hence forming high resolved images of either polarity A survey of the magnitudes of the various sources of blurring is given in Table 2

Mechanical design of the prototype chamber

A diagrammatic sketch is presented in Fig 2 and a photograph in Fig 3 of the ionography chamber which gives images up to 28 cm in diameter The electric connections gas and pump connections appear in Fig 4

The lower electrode to which the high tension is applied is spherically curved to a radius of 101 cm and is made of solid brass The gradual curvature of the outer edge and of the metal ring above it was designed to maintain uniform spherical geometry in the imaging field to as large a radius as possible The upper electrode connected to earth is formed by the conductive aluminium backing of the imaging foil The latter was usually Mylar some 50 μm thick The foil is placed over the metal ring and is clamped between the O rings when the top plate is placed in position above the foil The electrode spacing in normal use is 1 5 cm but an additional perspex spacing ring was constructed which allowed experimental tests to be made at 4 5 cm spacing

The radiation window is a circular plate 9 mm thick made of carbon fibre composite material (manufactured by Composite Materials Bristol) which has an allowed workin stress of approximately 100 MPa Making the conservative assumption that the plate is freely supported between its steel clamping rings the chamber can be operated up to a pressure of 0 5 MPa with a factor of safety of 4 The measured transmission efficiency of the window is illustrated in Fig 5 for tube potentials from ^0 to 100 kV

Fig 3 Photograph of the ionography chamber with hydraulic closure system

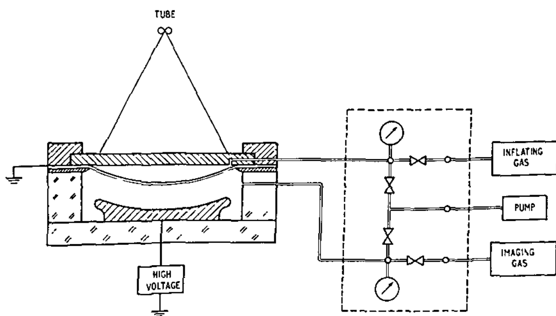


Fig 4 Electric connections and gas supplies for the ionography chamber

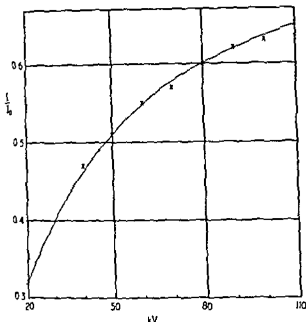


Fig 5 Transmission coefficient (I/I_0) for a 9 mm thick carbon fibre composite radiation window I_0 = incident exposure rate I = emerging exposure rate

The cylindric outer wall of the chamber and the base plate are made of perspex and are mounted on a steel platform which also supports 4 hydraulically operated jacks These jacks act on hinged clamping plates each having two pressure points on the steel ring clamping the top window The maximum pressure in the hydraulic jacking system is 17 MPa This system allows the imaging chamber to be closed or opened smoothly and rapidly

The foil is inflated to the correct curvature by passing nitrogen—a relatively non absorbing gas—into the space between foil and top plate The desired curvature is easily reproduced accurately by noting the additional compression of the imaging gas brought about by inflating the foil When this compression ratio had once been calibrated carefully the correct foil curvature could be reproduced rapidly and accurately in routine operation of the chamber This method also lends itself to automation

Development method

All the images presented in this report were developed by a simple powder-cloud technique (DESSAUER & CLARY 1965) The powder aerosol was produced by blowing puffs of powder through a fine nozzle into the development chamber (Fig 6) Xerox System 125 powder was used throughout Each puff of powder is injected horizontally and bouncing off the cylindric walls it forms eddies which produce a fairly even powder distribution in the upper part of the chamber A baffle above the jet prevents powder being blown directly to the foil An insulated grid to which a potential can be applied

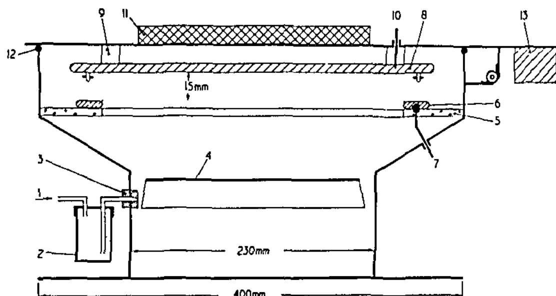


Fig 6 Sectional view of the development box 1 = gas inlet 2 = powder container 3 = nozzle 4 = baffle 5 = insulating support for grid 6 = grid 7 = high potential connection to grid 8 = foil holder 9 = insulating support for foil holder 10 = high potential connection to foil holder 11 = air filter 12 = rubber seal 13 = counterweight

allows the average field near the foil to be controlled and this determines the powder density deposited on the highly charged background which has been exposed to the unattenuated radiation beam outside the object Experience demonstrated that the best images were obtained when background powdering was suppressed or at least greatly reduced by applying a potential of a few kV to the grid or to the conductive backing of the foil The grid was some 15 mm from the foil and so was not designed to eliminate edge contrast in the image after the manner of a development electrode (DESSAUER & CLARK) The enhanced contrast which this development method yields at any sharp steps in charge density has been discussed in detail elsewhere (BOAG 1973 JOHNS et coll 1975) This edge contrast is most marked in the early stages of development and in the majority of the images development was stopped when less than 5 per cent of the average image charge had been neutralised by the oppositely charged powder The optical density of the powder coating in areas away from an edge was then often no more than 0 1 which is not nearly sufficient to give a good image density by transmitted light Images developed for edge contrast must therefore be viewed in strong oblique lighting when the edges appear bright by scattered light A permanent record on 35 mm film was produced by photographing the obliquely illuminated images inside a matt black box designed to eliminate disturbing reflections in the aluminium backing of the foil

Sensitivity In the present experimental work the compound CF_3Br commercially known as Freon 13 B1, was used as imaging gas It is cheap enough to be run to waste after imaging This avoided the need for an expensive recovery and purification



Fig 7 Ionographic image of child s foot (removed at operation) 1?5 μm foil 1.0 kV 8 mAs

system for xenon and allowed an examination of all aspects of the ionography system except its absolute sensitivity The photoelectric absorption cross section of xenon being so much larger than that of bromine a considerable increase in charge deposited per roentgen incident can be achieved by using xenon instead of CF_3Br The ratio of the sensitivity of xenon to that of Freon 13 B1 for imaging taking account of all the factors involved has been examined in detail by DANCE & BOAG (1977) for a

Table 3

Relative sensitivity of Xe and Freon 13 B1 for imaging (DANCE & BOAG *1977*)

Gas pressure (p) electrode spacing (d) (kPa m)	Tube potential (kVp) and filtration (mm)				
	30 0 5 Al	40 0 03 Mo	70 3 Al	90 3 Al	1?0 4 Al
pd 5 $\frac{Xe}{Freon}$	1 45	1 55	2.76	3 18	3 88
pd = 10 $\frac{Xe}{Freon}$	1 47	1 51	2 49	2 93	3 67
pd 10 for Xe pd = 5 for Freon	2.4	2.5	4 6	5.5	7 0



Fig 8 Ionographic image of human shoulder 120 kV 50 mAs fine focus Normal

range of roentgen ray energies and for two values of the product gas pressure × electrode spacing (p × d) viz pd = 5 kPa m and pd = 10 kPa m (Table 3) They differ appreciably from the imaging efficiency values calculated by FENSTER et coll (1974) because the data in Table 3 take into account the hardening of the radiation which occurs in its passage through 10 cm of tissue plus the carbon top plate It can be seen that for equal values of the product p × d xenon should be only 1 5 times as sensitive as Freon 13 B1 for filtered 40 kV radiation but this sensitivity ratio rises to 3 for 90 kV radiation and to nearly 4 for 120 kV radiation In the experiments pd = 6 5 kPa m was generally used In an improved design of chamber this could easily be raised to pd = 10 kPa m Consequently by using xenon at slightly higher pressure it might be expected to get about 5 times as high imaging sensitivity as achieved in the present experiments at 90 kV and nearly 7 times as high with 120 kV radiation This has to be borne in mind when considering the exposure factors used for the images presented in this report

The development method used and the special properties of the toner as the developing powder is called, also strongly influence the overall sensitivity of the system A more efficient toner will produce a visible image from a latent one having less than the normal charge density Toner efficiency depends inter alia upon the toner particles having a low ratio of charge to mass A toner suitable for edge contrast

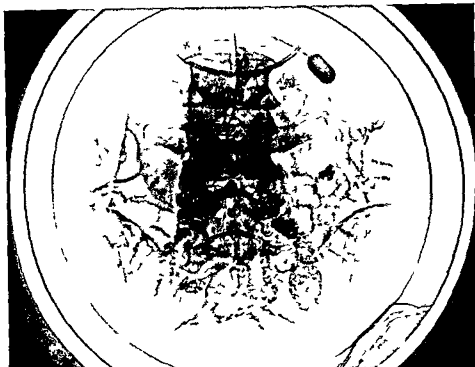


Fig 9 Lower abdominal view with enlarged pelvic lymph node Crosby capsule and tube 120 kV 80 mAs fine focus

development may not be the best for complete neutralisation of the charge variation to yield a density image Liquid toners (i e colloidal suspensions of fine toner particles) appear to be the most efficient for complete development However in many radiographic images practically all the diagnostic information is conveyed by the outlines of structures and no advantage is then to be derived from developing out to yield a density image

Another factor in sensitivity is the efficiency with which the ions formed in the imaging gas can be collected on the foil The conditions governing ionic recombination in the noble gases xenon and krypton or in mixtures of these with Freon 13 B1 have been investigated exhaustively (BOAG et coll 1975 SEELENTAG et coll 1976) and the effect of the many parameters involved—exposure rate gas pressure electrode spacing collecting potential etc —have been incorporated into general formulae from which collection efficiency can be calculated In general the loss of ions from this cause can be kept below 20 per cent provided a collecting potential of some 10 to 20 kV is maintained across a gas space not much larger than 1 cm

In principle sensitivity should be increased by using a thick dielectric layer as charge collector instead of a thin foil for this will increase the field strength above



a b

Fig. 10. Ionographic images of a model head taken at 60 kV, 140 mAs with Freon at 0.43 MPa. a) With 1.5 cm electrode spacing and b) with 4.5 cm electrode spacing.

the charge pattern during development. This idea has in fact been used to increase the sensitivity of autoionography images of radioactive spots on thin layer chromatography plates (BARISH & BOAG 1978). However, this method is not satisfactory with the complex low contrast images encountered in medical radiology (SEELENTAG et coll. 1978). Foils of 100 to 200 μm thickness are satisfactory but anything much thicker than this degrades resolution, as confirmed experimentally.

Examples of clinical ionographic images

Exposure procedure. Since the roentgen apparatus (Siemens Tridoros 5S) and the ionographic chamber were two separate units, great care had to be taken in aligning them at the correct focus to chamber distance (1 m). Alignment accuracy was checked before each session by a special tubular jig resting on, and perpendicular to, the top plate and accurately concentric with the ring supporting the imaging foil. This tube carried fine cross wires at each end. An ionographic image was taken and adjustments made until the crossing points of the two pairs of cross wires coincided. The patient, lying on a movable top diagnostic couch, was then slid into position and the clinical image exposed.

Alignment checking would be unnecessary in a rigidly linked system and other

steps in the process of imaging such as preparing the foil and filling and emptying the chamber could readily be automated in a fully engineered equipment

Ionographic images taken with the equipment described using the normal electrode spacing of 1 5 cm appear in Figs 7 to 9 An image of a skull phantom taken with an additional spacing ring inserted into the chamber to give an interelectrode gap of no less than 4 5 cm is reproduced in Fig 10 It is remarkable that with an absorbing layer as thick as this the resolution has only fallen to about 4 line pairs per mm

Ionography lends itself easily to taking subtraction images It is only necessary to give a double exposure the first one with positive polarity on the ionography chamber electrode the second with negative polarity The charge collected during the first exposure will be exactly neutralised by that collected in the second except in those parts of the image where movement of any kind has occurred The developed image will thus show only parts which have moved If the second exposure is slightly shorter than the first these parts will be seen against a dim background over the rest of the image Clinical subtraction images have not yet been produced but it has been confirmed that the technique is practicable using static models moved between exposures

Conclusions

The feasibility of ionography in medical radiology has been explored using a very simple prototype ionization chamber The images obtained closely resemble those produced with xeroradiography when powder cloud development is used but they are produced at a considerably lower level of radiation exposure to the patient Development rather than latent image formation is the factor which limits sensitivity so further improvement may be possible

Acknowledgements

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SUMMARY

The design and construction of an experimental ionography chamber are described and the principles of this new electrostatic imaging technique are discussed Examples of medical ionographic images taken with this simple prototype chamber are presented

ZUSAMMENFASSUNG

Der Entwurf und die Konstruktion einer experimentellen ionographischen Kammer werden beschrieben und die Prinzipien dieser neuen elektrostatischen Bildtechnik diskutiert Beispiele von medizinischen ionographischen Bildern die mit dieser einfachen Prototypkammer hergestellt worden sind werden gegeben

RESUME

Les auteurs décrivent le plan et la construction d'une chambre expérimentale d iono graphie et les principes de cette nouvelle technique électrostatique d imagerie Ils donnent des exemples d images ionographiques médicales prises avec cette chambre prototype simple

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VISUAL EVALUATION OF MICROSCOPIC MOTTLE

K SELIN and S REICHMANN

Several methods have been used in attempts to determine the image quality of intensifying screens or screen film combinations A simple method of assessing certain properties of a screen has been the subjective evaluation of the imaging of different test objects e g wire meshes holes and low contrast objects of various sizes (NELSON 1949 ROSSMANN 1966) Another similar method has been the determination of the resolution (line pairs/mm) of the screen Since these methods are mainly subjective attempts were early made to devise more objective methods

From the field of optics the concept of modulation transfer function (MTF) was adopted (MORGAN 1962 ROSSMANN 1962 ROHLER 1965) For intensifying screen this function may be regarded as a measure of the spread of light within the screen obtainable in the following way A knife edge or a narrow slit is imaged by a screen on a single emulsioned film the density across the image being measured with a microdensitometer with the slit opening parallel to the image (ROSSMANN 1964) By means of a mathematical procedure including a Fourier analysis the MTF is calculated The densities measured must be noise independent to obtain reproducible values for the MTF This may be accomplished by using a rather narrow slit of considerable length producing a mean value of the density within the slit If the slit image is recorded on a film of low speed as compared with conventional roentgen films a further noise reduction is obtained The light emitted from a screen when exposed through a slit may also be used directly for MTF measurements as in the Odeta MTF Analyzer (from Oude Delft Holland) (HOLJE & SVAHN 1974)

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Each density fluctuation in the image which derives from an actual attenuation difference within an object may be looked upon as a signal. Even when no attenuation differences are present, certain fluctuations in image density are always to be expected in clinical radiography owing to the relatively small number of roentgen photons per unit area, the photons being randomly distributed. These fluctuations may analogously be looked upon as noise (quantum noise or quantum mottle) which tends to obscure the perception of the signals (MORGAN 1965). Certain other types of noise may also be encountered besides the quantum mottle (CLEARE et coll. 1962, ROSSMANN 1963, REICHMANN & HELANDER 1974). The contrast of a signal generally has to exceed the background mottle by a certain factor (ROSE 1973) if visibility of the signal is to be ensured. This means that the ratio between signal and noise is the crucial factor determining visibility in this respect.

It has been clearly demonstrated that neither of the parameters mentioned can be used to predict the imaging properties of a screen for all kinds of objects. ROSSMANN (1966) for instance, comparing two screen film combinations with different MTF, found that the combination with the lower MTF had the best properties for depicting large sized objects of low contrast, this type of object being limited by the signal/noise ratio rather than by the MTF. On the other hand, it is generally held (ROSSMANN 1966) that depiction of narrow slits with high attenuation differences is limited mainly by the MTF, noise thus being of minor importance. However, the latter type of depiction has to a large extent been investigated by means of the noise independent techniques used in MTF evaluations, and so the actual influence of noise has remained unestablished. ROSE, describing image quality in TV systems, emphasized the fact that in images built up by a small number of informative elements, even resolution may be limited by noise rather than by MTF. Clinical radiography employs a limited number of photons, which means that the conditions described by ROSE may be valid.

The type of object detail that is the most difficult to demonstrate in clinical radiography is neither a slit with a high attenuation difference (MTF limited) nor large objects with a low attenuation difference (noise limited), but small details with a low attenuation difference. Obviously MTF and noise should be expected to interact in determining visibility for this type of object. Each of these parameters can be measured separately. However, no mathematical concept describing their interaction exists (ROSSMANN 1974, WAGNER 1977). In the present report a technique for direct visual evaluation of this interplay is described.

Preliminary method. Obviously direct visual evaluation of the influence of noise on the imaging of a narrow slit makes magnification necessary. It might be supposed that microscopy would be useful, but it was found that the proper granularity of the film made demonstration of the mottle fluctuations of density almost impossible despite that they were coarser than the granularity (Fig. 1 a). Furthermore, with a double emulsioned film it is only possible to see one layer at a time, the interaction



a



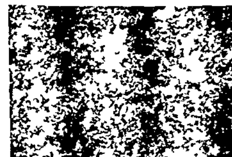
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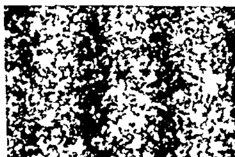
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d



e



f

Fig 1 Magnified grid images displaying the effect of the copying procedure where a grid image on a double-emulsioned film is contact copied onto a single-emulsioned fine grained film Single emulsioned roentgen films have been used to analyse the two layers of the double-emulsioned film separately a) Magnification of a single-emulsioned film with grid image without previous copying b c) Single emulsioned film copied onto Agfa Gevaert Graphic film N 33 the emulsion in contact with and turned away from the N 33 film respectively d) Double-emulsioned film copied onto N 33 e f) Same as (c) and (d) but using Kodalith Ortho Type 3 instead of N 33 In (a) the inherent granularity of the original film makes evaluation of the density fluctuations almost impossible d) demonstrates the joint effect of the varying degree of filtration of the two emulsions (b and c) at the copying The best recording of the density fluctuations (microscopic mottle) is obtained with the Kodalith film probably due to its higher contrast and finer grain Kodak X-omatic screens and Curix RP 1 have been used for the original grid images

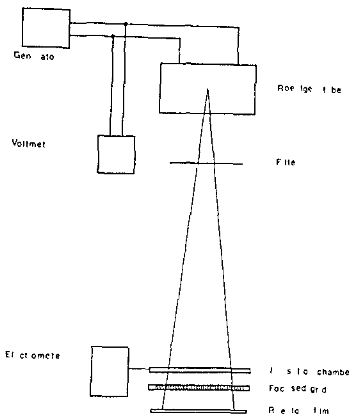


Fig 2 The exposure arrangement including tube grid cassette and devices for measurement of tube potential and (relative) incident radiation dose

of the two layers being inaccessible to analysis By chance these obstacles were found to be eliminated if the original roentgen film was contact printed onto a film of finer grain (Fig 1 d) This film yielded a less disturbing granularity yet the granularity of the original film was to a large extent lost In technical terms this is equivalent to a filtration of high spatial frequencies i e the printing acts as a low pass filter Fig 1 d was obtained in the following way

A focused grid (FFD 110 cm 44 lead bars/cm) was chosen as test object yielding a series of parallel slits The grid was tested according to the method of STRID (1976) for ruling out possible manufacturing defects The grid and the tube were placed in fixed positions An ionisation chamber connected to an electrometer was placed in front of the grid for relative dose measurements Tube potential was measured directly on the secondary side of the generator The experimental set up is illustrated in Fig 2 In all the following experiments tube potential was 90 kV and added filtration 2 mm Cu An image of the grid was then taken using Kodak Regular screens and Curix RP 1 film (average density 1 0) which was developed in a roll machine used in routine work (Pakorol developer Agfa Gevaert G 138 26 C process time 2 5 min) A contact print of this film was then obtained on Agfa Gevaert N 33 Graphic film, using an ordinary copying frame (lamp film distance 100 cm) and an ordinary incandescent bulb (25 W) The print was developed in a roll machine (Pakorol developer Agfa Gevaert G 122 31 C, process time 6 min) In order to demonstrate



Fig 3 Photomicrography of the output image of a fibre optics plate placed on a single-emulsioned film with grid image (same as in Fig 1) A mottle of the same type as in Fig 1 d appears proving that the copy ing process reveals information in herent in the original film

small details in the print invisible at direct inspection the copy was exposed (×32) in a Zeiss photomicroscope Exposure time was controlled by a photo timer meas uring the whole view field area Recording was made on Agfapan 25 a 35 mm fine grained black and white film with suitable contrast developed in the same way as the N 33 film but with a process time of 2 5 min The resulting grid image (Fig 1 d) clearly demonstrates that the transition between dark and bright lines was not constituted by such parallel zones as might be expected if a diffuse spread of light had been the only factor determining the definition of the line image Instead the transition zone had a wavy appearance and the lines themselves looked more or less fragmented as if there had been a microscopic mottle

Testing of the preliminary method In the method described many parameters might affect the final image Therefore several experiments had to be performed in order to eliminate possible false information being added or pertinent information being lost at the different steps Thus not until it had been proved that the final image carried relevant information from the original grid film could a discussion take place as to how the final image was built up

Whether the microscopic noise of the processed image emanated from the original film or whether it was a side effect of the copying was tested by another type of filtra tion A fibre optics plate was placed on a single-emulsioned original grid film the output image of the fibre optics being exposed in the photomicroscope (Fig 3) A single-emulsioned film was used since the fibre optics transmits information from the adjacent emulsion only Details smaller than the cross section of a fibre cannot be resolved leading to elimination of film granularity A mottle of the same type as in Fig 1 d was visible In the fibre optics image the mottle was less apparent Experi ments (described in the following) suggest the difference to be due to the fact that Fig 3 was obtained from one emulsion only (cf Fig 1 b) Thus the copying implied a filtration which revealed information inherent in the original film

The next step involved a test of certain factors

Original film
- Agfa Gevaert Curix RP 1
- Ilford Red Seal (same speed as Curix)
- Agfa Gevaert Medichrome (lower speed very fine grain)

Development of original film
- Roll machine
- Manual (Agfa Gevaert G 150 20 C 5 min)

Number of emulsions in the original film and mode of copying
- Two emulsions
- One emulsion next to copying film
- One emulsion away from copying film

Light source for the copying
- Opaque standard bulb (lamp film distance 100 cm)
- Clear lamp point formed filament (lamp film distance 100 cm)

Copying film
- Agfa Gevaert N 33 Graphic film
- Kodak Kodalith Ortho Type 3 (*higher resolution higher contrast)*
- Kodak MR plates (extreme resolution high contrast)

The different factors were varied according to the alternatives given and the first *alternative in each group represents the preliminary method It was noted whether* or not the exchange significantly affected the final magnified image For the Curix and Red Seal *films all possible combinations were tested the Medichrome film* being more sparsely tested

As original film the Medichrome possibly gave somewhat higher precision the other two films being equal However the difference was considered insignificant Yet despite its specific properties (finer transparent grains) the Medichrome film yielded the same microscopic mottle as the other two films thus indicating that the mottle is not just a film artifact Development of black and white films did not improve by manual processing Machine development was thus preferred The two types of light sources gave the same appearance to the copies even if a single emulsioned film was copied having its emulsion turned away from that of the copying film The standard bulb with its higher luminosity was therefore preferred

The tests with *the single emulsioned original films were performed to find out* how the two layers of a radiographic film were depicted on the single coated copying film Single *emulsioned films* were obtained by *using one screen* and developing only the layer next to the screen (SELIN & REICHMANN 1977) With the emulsion next to the copying film almost too much of the granularity of the original film was depicted on the Kodak MR plates due to the extreme resolution of these plates while the

granularity was less apparent for the films with lower resolution (Fig 1 b) With the emulsion not in contact with the copying film increased filtration was obtained due to diffusion of light in the roentgen film base yet the main features of the microscopic mottle were retained (Fig 1 c) The high contrast of the Kodalith film turned out to be advantageous as many details were more easily observable The grains in the Kodalith film were also less disturbing at magnification as compared with N 33 (cf Fig 1 c and e) After these tests the copying film was changed to Kodalith Fig 1 d and f show the images when exposing with double screens on two emulsions (N 33 and Kodalith respectively) These images are obviously the summation of two differently filtered images one from each emulsion The evaluation of the bright and dark lines seems easier in the Kodalith film and in the following when speaking about copies from grid films this kind of image is being considered

Final method The following procedure represents the final technique for producing *grid images*

Object
Focused grid FFD 110 cm 44 lead bars/cm ratio 1 10

Recording
Screens to be tested
Film Curix RP 1 (Agfa Gevaert) machine development (developer Agfa Gevaert G 138 26 C 2 5 min) Both emulsions exposed and developed

Copying
Copying frame ordinary opaque bulb lamp film distance 100 cm
Film Kodalith Ortho Type 3 (Kodak) machine-development (developer Agfa Gevaert G 122 31 C 2 5 min)

Enlargement
Photomicroscope magnification 32 phototimer integrating the whole image area
Film Agfapan 25 development same as Kodalith

Discussion

Evaluation of the MTF of a screen film combination implies microdensitometry of a slit image However it is theoretically possible to construct slit images which differ in density distribution but which still give the same densitometric values when measured with a narrow fairly long slit (Fig 4) Thus these values alone do not provide full information about small density variations In the slit images (Fig 5 a b) noise is clearly visible This noise invisible without enlargement may thus be called microscopic Certainly the noise may be measured microdensitometrically in order

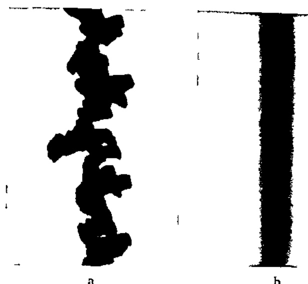
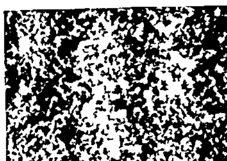


Fig 4 Two constructed slit images chosen to demonstrate that the density variations when measured with a long narrow slit across the image might well be the same in two images despite completely different density distributions

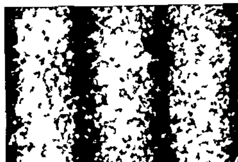
to yield a Wienerspectrum However, no methods exist for describing the effect of this noise on sharpness Therefore the initial procedure chosen for the analysis of this interplay is a qualitative visual evaluation after magnification With a fast screen the definition of the grid lines is mainly noise limited (Fig 5 a) with a considerable *fragmentation of the dark lines (lead bar image) With a high definition screen* needing a 25 fold dose increase as compared with the fast screen a qualitatively different definition is obtained (Fig 5 b) This is even more marked without screens using industrial film (Fig 5 c)

In the copying procedure a contact copy is produced containing information from both emulsions of the original roentgen film This means that the two mottles of the double emulsioned film are projected onto each other in the same way as in direct *inspection of the film The image recorded in the original emulsion not facing* the copying film thus undergoes a certain frequency filtration but only to an insignificant degree so that the mottle is mainly unchanged (Fig 1 c) If only one emulsion were copied only half the actual mottle would be taken into account resulting in an underestimation of the influence of the mottle for the definition of image details (Fig 1 b d) On the other hand the image recorded in the emulsion not facing the copying film gets a lower MTF at the copying due to spread out of light However this does not constitute a significant source of error since what is to be evaluated is mainly the qualitative appearance in the transition between dark and bright bands If this zone is wavy and fragmented mottle is assumed to be of significance for the definition of the lines (Fig 5 a) if not mottle is probably less important (Fig 5 b)

High contrast objects have previously been used for measurement of unsharpness (ROSSMANN 1964 HOLJE & SVAHN) The same type of object namely a grid was used in the present investigation It is easier to analyse the influence of a microscopic noise by means of a high contrast object Even if the results cannot be directly applied to biologic structures, i e small low contrast details it is evident that the disturbing



a



b



c

Fig 5 Grid images from a) a very fast screen (Agfa Gevaert MR 600) and b) a slow screen (Kodak X-omatic Fine) representing two extreme situations when screens of varying speed are used A 25 fold dose increase is needed in (b) as compared to (a) In (a) there is a considerable fragmentation of the dark lines (lead bar images) due to a microscopic mottle This mottle is less important in (b) In (c) an almost ideal depiction of the grid is obtained by using non screen industrial film

effect of the noise must be still more deleterious for the depiction of this type of object The present grid has roughly 4 lines/mm This frequency may be expected to discriminate well between fast and slow screens as is also suggested in Fig 5 a and b

A more thorough discussion of how the grid image is built up will be given in a subsequent report (SELIN & REICHMANN to be published) in which screens with different phosphors exposed at various tube potentials and various exposure levels are investigated with the method described

SUMMARY

According to ROSE the resolution of an imaging system is under certain conditions limited by noise rather than by the finite geometric response as expressed by the modulation transfer function In order to investigate whether this applies to clinical radiography as well a technique for magnification of roentgen films has been devised making possible visual evaluation of microscopic noise

ZUSAMMENFASSUNG

Entsprechend ROSE wird die Auflosung eines Abbildungssystems unter gewissen Bedingungen mehr durch das Rauschen als durch begrenzte geometrische Antwort ausgedrückt durch die Modulations Transfer Funktion bestimmt Um festzustellen ob das auch fur die klinische Rontgenologie zutrifft wurde eine Technik zur Vergrosserung von Rontgenfilmen ausgearbeitet die es ermoglicht mikroskopisches Rauschen festzustellen

RESUME

D'après Rose la résolution d'un système d'imagerie est dans certaines conditions limitée par le bruit plutot que par la réponse géométrique finie exprimée par la fonction de transfert de modulation. Pour rechercher si ceci s'applique aussi à la radiographie clinique, les auteurs ont mis au point une technique d'agrandissement des films radiographiques permettant l'appréciation visuelle du bruit microscopique.

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